GenCore version 5.1.6

OM protein - protein search, using sw model

Run on: July 2, 2003, 15:20:59 ; Search time 68 Seconds
(without alignments)
4606.944 Million cell updates/sec

Title: NP_000123
Perfect score: 12418
Sequence: 1 mqielstcfflellrfcfsa.....vvhqialrmevlgceaqdly 2351

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 908470 seqs, 133250620 residues

Total number of hits satisfying chosen parameters: 908470

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 200 summaries

Database : A_Geneseq_101002:*
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Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	12418	100.0	2351	6	AAP50059	Human factor VIII.
2	12418	100.0	2351	18	AAW11329	Native Factor VIII
3	12418	100.0	2351	19	AAW46245	Human factor III p
4	12418	100.0	2351	19	AAW44373	Human Factor VIII.
5	12418	100.0	2351	21	AAY52537	Human full-length
6	12414	100.0	2351	18	AAW11435	Active Factor VIII
7	12414	100.0	2351	18	AAW11416	Active Factor VIII
8	12414	100.0	2351	18	AAW11343	Active Factor VIII
9	12413	100.0	2351	18	AAW11461	Active Factor VIII
10	12413	100.0	2351	18	AAW11445	Active Factor VIII
11	12413	100.0	2351	18	AAW11425	Active Factor VIII
12	12413	100.0	2351	18	AAW11419	Active Factor VIII
13	12413	100.0	2351	18	AAW11398	Active Factor VIII
14	12413	100.0	2351	18	AAW11387	Active Factor VIII
15	12413	100.0	2351	18	AAW11362	Active Factor VIII
16	12412	100.0	2351	9	AAP81113	Factor VIII encode
17	12412	100.0	2351	9	AAP80659	Sequence of human
18	12412	100.0	2351	18	AAW11437	Active Factor VIII
19	12412	100.0	2351	18	AAW11427	Active Factor VIII
20	12412	100.0	2351	18	AAW11408	Active Factor VIII
21	12412	100.0	2351	18	AAW11347	Active Factor VIII
22	12412	100.0	2351	18	AAW11332	Active Factor VIII
23	12411	99.9	2352	18	AAW11396	Active Factor VIII
24	12411	99.9	2351	18	AAW11371	Active Factor VIII
25	12409	99.9	2351	17	AAW00465	Factor-VIII. Homo
26	12409	99.9	2351	18	AAW11454	Active Factor VIII
27	12409	99.9	2351	22	AAB48843	Human factor VIII,
28	12408	99.9	2351	18	AAW11399	Active Factor VIII
29	12408	99.9	2351	18	AAW11404	Active Factor VIII
30	12407.5	99.9	2352	18	AAW11456	Active Factor VIII
31	12407.5	99.9	2352	18	AAW11458	Active Factor VIII
32	12407.5	99.9	2352	18	AAW11459	Active Factor VIII
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37	12407.5	99.9	2352	18	AAW11442	Active Factor VIII
38	12407.5	99.9	2352	18	AAW11447	Active Factor VIII
39	12407.5	99.9	2352	18	AAW11450	Active Factor VIII
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73	12407.5	99.9	2352	18	AAW11336	Active Factor VIII
74	12407.5	99.9	2352	18	AAW11337	Active Factor VIII
75	12407	99.9	2351	18	AAW11352	Active Factor VIII
76	12406	99.9	2351	18	AAW11468	Active Factor VIII
77	12406	99.9	2351	18	AAW11377	Active Factor VIII
78	12403.5	99.9	2350	18	AAW11376	Active Factor VIII
79	12403.5	99.9	2350	18	AAW11358	Active Factor VIII
80	12403.5	99.9	2350	18	AAW11359	Active Factor VIII
81	12402	99.9	2351	18	AAW10591	Factor VIII:C (Phe
82	12402	99.9	2351	18	AAW13496	Factor VIII:C (Arg
83	12402	99.9	2351	20	AAY21676	Factor VIII protei

84	12400	99.9	2351	18	AAW10592	Factor VIII:C (Tyr
85	12400	99.9	2351	18	AAW11471	Active Factor VIII
86	12399.5	99.9	2350	18	AAW11413	Active Factor VIII
87	12399	99.8	2349	18	AAW11443	Active Factor VIII
88	12399	99.8	2351	18	AAW11472	Active Factor VIII
89	12398	99.8	2349	18	AAW11424	Active Factor VIII
90	12398	99.8	2349	18	AAW11373	Active Factor VIII
91	12398	99.8	2351	18	AAW10590	Factor VIII:C (Phe
92	12397.5	99.8	2350	18	AAW11405	Active Factor VIII
93	12397.5	99.8	2350	18	AAW11346	Active Factor VIII
94	12396.5	99.8	2350	18	AAW11470	Active Factor VIII
95	12396.5	99.8	2350	18	AAW11375	Active Factor VIII
96	12396	99.8	2351	16	AAR70223	Human Factor-VIII:
97	12395	99.8	2349	18	AAW11460	Active Factor VIII
98	12395	99.8	2351	15	AAR56352	Sequence of human
99	12394.5	99.8	2350	18	AAW11457	Active Factor VIII
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102	12393	99.8	2349	18	AAW11465	Active Factor VIII
103	12393	99.8	2349	18	AAW11430	Active Factor VIII
104	12393	99.8	2349	18	AAW11366	Active Factor VIII
105	12392.5	99.8	2348	18	AAW11395	Active Factor VIII
106	12392	99.8	2349	18	AAW11428	Active Factor VIII
107	12392	99.8	2349	18	AAW11420	Active Factor VIII
108	12392	99.8	2349	18	AAW11338	Active Factor VIII
109	12392	99.8	2351	8	AAP70448	Human factor VIII:
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124	12385.5	99.7	2348	18	AAW11414	Active Factor VIII
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150	12366.5	99.6	2344	18	AAW11361	Active Factor VIII
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157	12356	99.5	2343	18	AAW11393	Active Factor VIII
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160	12344.5	99.4	2342	18	AAW11349	Active Factor VIII
161	12339	99.4	2351	7	AAP60741	Sequence of human
162	12314	99.2	2332	22	AAB71902	N-terminal truncat
163	12311	99.1	2332	18	AAW33223	Procoagulant-activ
164	12306	99.1	2332	18	AAW33222	Procoagulant-activ
165	12306	99.1	2332	18	AAW33225	Procoagulant-activ
166	12303	99.1	2332	18	AAW33224	Procoagulant-activ
167	12301	99.1	2332	14	AAR43257	Human Factor VIII.
168	12301	99.1	2332	19	AAW53483	Human factor VIII.
169	12301	99.1	2332	20	AAY31594	Human factor VIII
170	12301	99.1	2332	22	AAE10826	Human mature wild-
171	12301	99.1	2332	22	AAE11200	Human factor VIII
172	12301	99.1	2332	22	AAB50465	Human factor VIII.
173	12301	99.1	2332	23	AAU79869	Human factor VIII.
174	12297	99.0	2332	23	AAU79870	Human factor VIII
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177	12295	99.0	2332	23	AAU79871	Human factor VIII
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180	12283	98.9	2332	23	AAU79875	Human factor VIII
181	12261	98.7	2332	8	AAP71727	Facor VIII:c varia
182	12260	98.7	2332	8	AAP71729	Facor VIII:c varia
183	12258	98.7	2332	8	AAP71726	Facor VIII:c varia
184	12258	98.7	2332	8	AAP71728	Facor VIII:c varia
185	12251	98.7	2332	21	AAY57847	Human Factor VIII
186	12181	98.1	2332	19	AAW44132	Homo sapiens modif
187	11935	96.1	2351	6	AAP50319	Human antihaemophi
188	11080	89.2	2098	17	AAR86863	Factor-VIII. Homo
189	9493	76.4	2343	21	AAY57846	Canine Factor VIII
190	9481	76.3	2343	20	AAW80989	Canine factor VIII
191	8835	71.1	2319	19	AAW53485	Murine factor VIII
192	8835	71.1	2319	19	AAW44135	Mus musculus facto
193	8835	71.1	2319	20	AAY31596	Mouse factor VIII
194	8835	71.1	2319	22	AAB50467	Mouse factor VIII.
195	8828	71.1	2319	22	AAE11202	Murine factor VIII
196	8730	70.3	2304	21	AAY57848	Mouse Factor VIII
197	8357	67.3	1661	18	AAW18670	Factor VIII-dB695-
198	8076	65.0	2133	20	AAY31597	Porcine factor VIII
199	8076	65.0	2133	22	AAB50468	Porcine factor VIII
200	8070	65.0	2133	19	AAW44133	Sus scrofa factor

ALIGNMENTS

RESULT 1
AAP50059
ID AAP50059 standard; protein; 2351 AA.
XX
AC AAP50059;
XX
DT 27-OCT-1991 (first entry)
XX
DE Human factor VIII.
XX
KW Human factor VIII;
XX
OS Homo sapiens.
XX
PN EP160457-A.
XX
PD 06-NOV-1985.
XX
PF 18-APR-1985; 85EP-0302734.
XX
PR 20-APR-1984; 84US-0602312.
XX
PA (GETH) GENENTECH INC.
XX

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PI   Capon DJ, Vehar GA, Lawn RM, Wood WI;
XX
DR   WPI; 1985-277976/45.
DR   N-PSDB; AAN50054.
XX
PT   New recombinant functional human factor VIII or deriv. - useful for
PT   treating haemophilia and obtd. as pure prod. by recombinant DNA
PT   technology.
XX
PS   Disclosure; Fig. 10a(10-10C(III); 109pp; English.
XX
CC   The sequence is that of human factor VIII. Amino acids 1-19 are the
CC   predicted signal peptide, and amino acids 1-2332 are the predicted
CC   mature protein. The protein is produced in pure form and in useful
CC   amts. using recombinant DNA techniques. Factor VIII can be used
CC   to correct factor VIII deficient plasma, and activates factor X to
CC   Xa in the presence of factor IXa, Ca and phospholipid. These to
CC   activities are inactivated by antibodies specific for factor VIII.
CC   The activity of the prod. is bound to an immobilised monoclonal
CC   antibody specific for factor VIII. Factor VIII activity is
CC   activated by thrombin. The activity is bound to, and can be eluted
CC   from, immobilised von Willebrand factor. Dose of factor VIII is
CC   20-40 units/kg over 8 hours i.v. for maintenance therapy for
CC   haemophilia, 40 units/kg for preoperative conditions, or 15-20
CC   units/kg for minor haemorrhaging.
XX
SQ   Sequence  2351 AA;

  Query Match          100.0%;  Score 12418;  DB 6;  Length 2351;
  Best Local Similarity  100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
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Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

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Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
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Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
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Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
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Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
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Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy       2161 PPIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 PPIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
              ||||||||||
Db       2341 EVLGCEAQDLY 2351


RESULT 2
AAW11329
ID   AAW11329 standard; Protein; 2351 AA.
XX
AC   AAW11329;
XX
DT   17-NOV-1997  (first entry)
XX
DE   Native Factor VIII:C.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2351
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Region          1668..2350
FT                   /note= "light chain fragment"
FT   Domain          760..1667
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
DR   N-PSDB; AAT51357.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Disclosure; Fig 1; 90pp; English.
XX
CC   This sequence represents the native Factor VIII:C. Factor VIII:C is a
CC   large glycoprotein that participates in the blood coagulation cascade
CC   that ultimately converts soluble fibrinogen to insoluble fibrin clot,
CC   effecting haemostasis. A deficiency in Factor VIII:C is responsible for
CC   haemophilia A, which is an X-chromosome-linked inherited bleeding
CC   diathesis. Factor VIII:C is activated by plasma proteases, such as
CC   thrombin. During activation the mature polypeptide is cleaved to
CC   generate heavy and light chain fragments that are further cleaved. The
CC   DNA encoding this sequence is mutated, using mutagenic primers, to
CC   produce the active Factor VIII:C analogues of the invention (such as
CC   AAW11330). The analogues comprise a native Factor VIII:C polypeptide
CC   modified at a site adjacent to a non-activating Arg residue so that a
CC   Arg-Pro or Pro-Arg dipeptide is created. Complexes of two or more of the
CC   analogues, nucleic acids and vectors encoding them may be used alone or
CC   in conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2351 AA;

  Query Match             100.0%;  Score 12418;  DB 18;  Length 2351;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy         1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy        61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy       121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy       181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy       241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy       301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGRAHGPALLTKDNALFKVSISLLKTN 1020

Qy        1021 KTSNNSATNKKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1021 KTSNNSATNKKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy        1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy        1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEPTKDVGLKEMVFPSSRNLFLTNLDN 1200
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEPTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy        1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy        1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy        1321 SQQNFVTQRSKRALKQPRLPLEETELEKRIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1321 SQQNFVTQRSKRALKQPRLPLEETELEKRIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy        1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy        1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy        1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy        1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy        1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy        1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSPQKRTHRYFIAAVERLWDYGMSSSPHVLRNR 1740
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSPQKRTHRYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy        1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy        1801 PYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1801 PYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy        1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCRA 1920
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCRA 1920

Qy        1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy        1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy        2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy        2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy        2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy        2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy        2281 ISSSQDGHQWTLFPQNGKVKVFQGNQDSPTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2281 ISSSQDGHQWTLFPQNGKVKVFQGNQDSPTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy        2341 EVLGCEAQDLY 2351
               ||||||||||| 
Db        2341 EVLGCEAQDLY 2351

RESULT 3
AAW46245
ID   AAW46245 standard; Protein; 2351 AA.
XX
AC   AAW46245;
XX
DT   06-AUG-1998  (first entry)
```

```
XX
DE   Human factor III protein sequence.
XX
KW   Replication defective; recombinant retrovirus; RRV; therapeutic protein;
KW   haemophilia; thrombosis; hypercoagulable disorder; liver disease; human;
KW   hepatitis; thalassemia; phenylketonuria; Lesch-Nyhan syndrome; diabetes;
KW   cystic fibrosis; Duchenne's Muscular Dystrophy; hypercholesterolemi;
KW   hypopituitarism; adenine deaminase deficiency, HIV infection;, anaemia;
KW   Guacher's syndrome; high blood pressure; Alzheimer's disease, factor III;
KW   autoimmune; inflammatory disease.
XX
OS   Homo sapiens.
XX
PN   WQ9800541-A2.
XX
PD   08-JAN-1998.
XX
PF   02-JUL-1997;   97WO-US11784.
XX
PR   04-JUN-1997;   97US-0869309.
PR   03-JUL-1996;   96US-0645601.
PR   13-AUG-1996;   96US-0696381.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Allen JR, Barber JR, Boder M, Chang SMW, Chong K;
PI   De La VEGA D, Depolonj, Greengard J, Hsu DC, Ibanez CE;
PI   Jolly DJ, Lee R, Mittelstaedt DM, Prussak CE, Respess JG;
XX
DR   WPI; 1998-086966/08.
DR   N-PSDB; AAV19580.
XX
PT   New replication defective recombinant retro-viruses - which can be
PT   administered to provide long term systemic expression of therapeutic
PT   protein in blood, useful in, e.g. treating hyper-coagulable
PT   disorders
XX
PS   Example 28; Pages 203-210; 272pp; English.
XX
CC   This is the human factor III sequence. The encoding DNA is used in the
CC   construction of recombinant retroviral vectors expressing human
CC   factor VIII. The specification provides the preparation of replication
CC   defective recombinant retrovirus (RRV) expressing a therapeutic protein.
CC   The RRV preparation is resistant to degradation by human complement and
CC   is capable of inducing long term systemic expression of the therapeutic
CC   protein when administered intravenously to a human. The long term
CC   systemic expression results in a measurable level of the therapeutic
CC   protein being produced in the blood of the human for a period of at least
CC   30 days after the administration of the RRV vector preparation. RRV's can
CC   be used for in vivo delivery of therapeutic protein to treat, e.g.
CC   haemophilia A, haemophilia B, thrombosis, hypercoagulable disorders,
CC   liver diseases such as hepatitis, disorders such as thalassemia,
CC   phenylketonuria, Lesch-Nyhan syndrome, severe combined immunodeficiency
CC   (sCID), cystic fibrosis, Duchenne's Muscular Dystrophy, inherited
CC   emphysema, familial hypercholesterolemia, diabetes, hypopituitarism,
CC   adenine deaminase deficiency, alpha1-antitrypsin deficiency, Guacher's
CC   syndrome, anaemia, infections such as HIV infection, high blood pressure,
CC   Alzheimer's disease, autoimmune or inflammatory disease or graft versus
CC   host disease. RRV's are capable of surviving inactivation in human serum
CC   thereby allowing efficient gene transfer over prolonged periods of time.
XX
SQ   Sequence   2351 AA;

  Query Match          100.0%;  Score 12418;  DB 19;  Length 2351;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
```

```
Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYITRVLFQDNSSHLPAASY 1440
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYITRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
             ||||||||||| 
Db       2341 EVLGCEAQDLY 2351


RESULT 4
AAW44373
ID   AAW44373 standard; Protein; 2351 AA.
XX
AC   AAW44373;
XX
DT   20-JUL-1998  (first entry)
XX
DE   Human Factor VIII.
XX
KW   Factor VIII; blood clotting; haemophilia A; gene therapy;
KW   retrovirus; vector; human.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Domain          711..1694
FT                   /note= "B-domain"
XX
PN   WO9800542-A2.
XX
PD   08-JAN-1998.
XX
PF   02-JUL-1997;   97WO-US11785.
XX
PR   04-JUN-1997;   97US-0869309.
PR   03-JUL-1996;   96US-0641601.
PR   13-AUG-1996;   96US-0696381.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Allen JR,  Barber JR,  Boder M,  Chang SM,  Chong K;
PI   De La Vega D,  Depolo NJ,  Greengard J,  Hsu DC,  Ibanez CE;
PI   Jolly DJ,  Mittelstaedt DM,  Prussak CE, Respess JG;
XX
DR   WPI; 1998-086967/08.
DR   N-PSDB; AAV15359.
XX
PT   New replication defective recombinant retroviruses - which express B
PT   domain-deleted human factor VIII or human factor IX for the
PT   treatment of haemophilia
XX
PS   Example 28; Page 164-166; 236pp; English.
XX
CC   This polypeptide comprises human Factor VIII.  The invention
CC   relates to preparations of replication defective recombinant
CC   retrovirus (RV) expressing a B domain-deleted human Factor VIII
CC   protein, such as the SQN deletion mutant (see AAW44372), where the
CC   recombinant RV is capable of infecting human cells, is resistant
CC   to degradation by human complement and is capable of inducing
CC   long-term (at least 30 days and up to 6 months or longer
CC   post-injection) systemic expression of Factor VIII when
CC   administered to a haemophilia A patient.
XX
SQ   Sequence   2351 AA;

  Query Match          100.0%;  Score 12418;  DB 19;  Length 2351;
  Best Local Similarity  100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
```

```
Qy          61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy         121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy         181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy         241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy         301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy         361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy         421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy         481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy         541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy         601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy         661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy         721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy         781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy         841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy         901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy         961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
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Db         961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy        1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy        1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
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Qy        1141 QGPSPKQLVSLGPEKSVEQQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
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Db        1141 QGPSPKQLVSLGPEKSVEQQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy        1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
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Db        1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy        1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
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Db        1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy        1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
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Db        1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy        1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
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Db        1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy        1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
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Qy        1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
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Qy        1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
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Db        1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy        1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy        1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
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Qy        1801 PYSPYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
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Qy        1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
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Qy        1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy        1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy        2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
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Db        2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy        2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
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Db        2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy        2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
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Db        2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy        2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
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Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

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              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
              ||||||||||| |
Db       2341 EVLGCEAQDLY 2351


RESULT 5
AAY52537
ID   AAY52537 standard; Protein; 2351 AA.
XX
AC   AAY52537;
XX
DT   28-FEB-2000  (first entry)
XX
DE   Human full-length factor VIII.
XX
KW   Factor VIII; haemophilia; proteolysis; heavy chain; light chain;
KW   secretion; von Willebrand Factor; vWF; C2 domain; intron 22; inversion;
KW   non-functional; bleeding disorder; coagulation; treatment.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Peptide          1..19
FT                    /note= "Signal peptide"
FT   Protein          20..1708
FT                    /note= "Maximum length human factor VIII heavy chain"
FT   Protein          1709..2351
FT                    /note= "Human factor VIII light chain"
XX
PN   WO9959622-A1.
XX
PD   25-NOV-1999.
XX
PF   17-MAY-1999;   99WO-US10872.
XX
PR   20-MAY-1998;   98US-0082000.
XX
PA   (GETH ) GENENTECH INC.
XX
PI   Vehar GA;
XX
DR   WPI; 2000-053195/04.
DR   N-PSDB; AAZ38604.
XX
PT   New method for treating hemophilia A  -
XX
PS   Disclosure; Fig 9; 50pp; English.
XX
CC   This sequence represents the full-length human factor VIII. In
CC   this form, the protein is 300 kD in size with the domain structure
CC   A1-A2-B-A3-C1-C2. However, prior to secretion, this 300 kD protein
CC   is proteolysed into a heavy chain (A1-A2-B, with continued
CC   proteolysis within the B domain resulting in molecules of varying
CC   length) and a light chain (A3-C1-C2) that remains non-covalently attached
CC   to the heavy chain. Upon secretion, factor VIII is rapidly cleared from
CC   the circulation unless it is bound by the plasma protein von Willebrand
CC   Factor (vWF). Factor VIII binds to vWF through the light chain, with
CC   known binding sites at the N-terminus and within the C2 domain.
CC   Haemophilia A is frequently caused by an intron 22 inversion in the
CC   factor VIII gene, which separates the gene into two sections, exons 1-22
CC   becoming inverted and localised telomeric to the original site, while
CC   exons 23-26 remain isolated at the original site. Exons 23-26 a portion
CC   of the C1 and all of the C2 domains, without which factor VIII is
CC   non-functional. The factor VIII gene product of individuals with this
CC   mutation thus comprises domains A1-A2-B-A3 plus a fragment of C1, which
CC   on proteolysis is non-functional, resulting in a bleeding disorder. The
CC   invention relates to a novel method for treating haemophilia A in a
CC   mammal able to produce the factor VIII heavy chain. The method comprises
CC   administering to the mammal either an effective amount of factor VIII
CC   light chain, or a gene encoding it, and may be useful for treating
CC   patients such as those whose haemophilia A is caused by intron 22
CC   inversion. The recombinant factor VIII products of this invention are
CC   derived from well-characterised starting materials which therefore
CC   reduces the risk of pathogenic infection which was previously a problem
CC   when using donated plasma. Furthermore, the invention provides a more
CC   economic and potentially more effective treatment for haemophilia. There
CC   is also a need of providing factor VIII activity to patients who
CC   produce or are at risk of producing antibodies against full-length
CC   factor VIII.
XX
SQ   Sequence   2351 AA;

  Query Match          100.0%;  Score 12418;  DB 21;  Length 2351;
  Best Local Similarity  100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
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Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db        781 PENDIEKTDPWFARHTPMPKIQNVSSSDLLMLLRQSPTHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
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Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDANQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDANQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
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Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
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Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELERKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELERKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
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Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy       2161 PPIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 PPIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
              ||||||||||| 
Db       2341 EVLGCEAQDLY 2351


RESULT 6
AAW11435
ID   AAW11435 standard; Protein; 2351 AA.
XX
AC   AAW11435;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue S1311X.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2351
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Modified-site   1330
FT                   /label= Phe, Glu, Pro
FT   Region          1668..2350
FT                   /note= "light chain fragment"
FT   Domain          760..1667
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
```

```
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 30; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2351 AA;

  Query Match             100.0%;  Score 12414;  DB 18;  Length 2351;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2350;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEQGNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEQGNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLVRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db        1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy        1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy        1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy        1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy        1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy        1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920

Qy        1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy        1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy        2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy        2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy        2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy        2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy        2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy        2341 EVLGCEAQDLY 2351
               ||||||||||| 
Db        2341 EVLGCEAQDLY 2351


RESULT 7
AAW11416
ID   AAW11416 standard; Protein; 2351 AA.
XX
AC   AAW11416;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue A774X.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX

FH   Key             Location/Qualifiers
FT   Peptide          1..19
FT                    /note= "signal peptide"
FT   Protein          20..2351
FT                    /note= "mature Factor VIII:C"
FT   Region           20..1667
FT                    /note= "heavy chain fragment"
FT   Modified-site    774
FT                    /label= Phe, Glu, Pro
FT   Region           1668..2350
FT                    /note= "light chain fragment"
FT   Domain           760..1667
FT                    /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;  96WO-US11444.
XX
PR   11-JUL-1995;  95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 26; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inhetited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2351 AA;

  Query Match          100.0%;  Score 12414;  DB 18;  Length 2351;
  Best Local Similarity  100.0%;  Pred. No. 0;
  Matches 2350;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSPPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSPPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
```

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Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARNAWPKMHTVNGYVNRSLPGLIGCHRKSVVWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
Db        241 AASARNAWPKMHTVNGYVNRSLPGLIGCHRKSVVWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEQQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
Db       1141 QGPSPKQLVSLGPEKSVEQQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSPFSIRPIYLTRVLPQDNSSSKLPAASY 1440
Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSPFSIRPIYLTRVLPQDNSSSKLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKDDTILSL 1620
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKDDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
Db       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
Db       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
Db       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
Db       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
Db       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
Db       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
Db       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
Db       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
Db
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Db          2341 EVLGCEAQDLY 2351


RESULT 8
AAW11343
ID   AAW11343 standard; Protein; 2351 AA.
XX
AC   AAW11343;
XX
DT   17-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue S224X.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2351
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Modified-site   243
FT                   /label= Phe, Glu, Pro
FT   Region          1668..2350
FT                   /note= "light chain fragment"
FT   Domain          760..1667
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 10; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2351 AA;

  Query Match          100.0%;  Score 12414;  DB 18;  Length 2351;
  Best Local Similarity  100.0%;  Pred. No. 0;
  Matches 2350;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
```

```
Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEQQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEQQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLYQIDYNEKE 1380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLYQIDYNEKE 1380

Qy       1381 KGATTQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGATTQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSPQKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSPQKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
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Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
              |||||||||||
Db       2341 EVLGCEAQDLY 2351
```

RESULT 9
AAW11461
ID AAW11461 standard; Protein; 2351 AA.
XX
AC AAW11461;
XX
DT 20-NOV-1997 (first entry)
XX
DE Active Factor VIII:C analogue V1717X.
XX
KW Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW proteolytic cleavage.
XX
OS Homo sapiens.
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Peptide 1..19
FT /note= "signal peptide"
FT Protein 20..2351
FT /note= "mature Factor VIII:C"
FT Region 20..1667
FT /note= "heavy chain fragment"
FT Region 1668..2350
FT /note= "light chain fragment"
FT Domain 760..1667
FT /note= "B domain"
FT Modified-site 1736
FT /label= Phe, Glu, Pro
XX
PN WO9703195-A1.
XX
PD 30-JAN-1997.
XX
PF 09-JUL-1996; 96WO-US11444.
XX
PR 11-JUL-1995; 95US-0001025.
XX
PA (CHIR) CHIRON CORP.
XX
PI Cohen FE, Hung DT, Innis M;
XX
DR WPI; 1997-119050/11.
XX
PT Factor VIII:C analog modified adjacent to a non-activating Arg
PT residue - used in the treatment of haemophiliacs, by improvement of
PT haemostasis

```
XX
PS   Claim 36; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2351 AA;

  Query Match          100.0%;  Score 12413;  DB 18;  Length 2351;
  Best Local Similarity  100.0%;  Pred. No. 0;
  Matches 2350;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy        1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy       61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy      121 GVSYWKASEGAETDDQTSQRKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      121 GVSYWKASEGAETDDQTSQRKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy      181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy      241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy      301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy      361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy      421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy      481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy      541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy      601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy      661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy      721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
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Db      721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy      781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy      841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy      901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy      961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy     1021 KTSNNSANTNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1021 KTSNNSANTNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy     1081 NHMSNKTTSSKNMEMVQQKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1081 NHMSNKTTSSKNMEMVQQKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy     1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEPTKDVGLKEMVFPSSRNLFTNLDN 1200
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEPTKDVGLKEMVFPSSRNLFTNLDN 1200

Qy     1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy     1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy     1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy     1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy     1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy     1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy     1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy     1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
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Db     1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy     1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
```

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Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
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Db       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
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Db       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
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Db       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
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Db       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
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Db       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
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Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
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Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
             ||||||||||| 
Db       2341 EVLGCEAQDLY 2351


RESULT 10
AAW11445
ID   AAW11445 standard; Protein; 2351 AA.
XX
AC   AAW11445;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue L1643X.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2351
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Modified-site   1662
FT                   /label= Phe, Glu, Pro
FT   Region          1668..2350
FT                   /note= "light chain fragment"
FT   Domain          760..1667
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 32; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAY51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2351 AA;

  Query Match             100.0%;  Score 12413;  DB 18;  Length 2351;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2350;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db        301 RQASLEISPITFLTAQTLLMDLGQPLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDWVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDWVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLNLDN 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEQGNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 NACESNHAIAAINEQGNKPEIEVTWAKQGRTERLCSQNPPVXKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy       1801 PYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 PYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCRA 1920
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCRA 1920

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
              |||||||||||
Db       2341 EVLGCEAQDLY 2351

RESULT 11
AAW11425
ID   AAW11425 standard; Protein; 2351 AA.
XX
AC   AAW11425;
XX
DT   20-NOV-1997  (first entry)
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XX
DE  Active Factor VIII:C analogue T1308X.
XX
KW  Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW  fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW  plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW  proteolytic cleavage.
XX
OS  Homo sapiens.
OS  Synthetic.
XX
FH  Key             Location/Qualifiers
FT  Peptide         1..19
FT                  /note= "signal peptide"
FT  Protein         20..2351
FT                  /note= "mature Factor VIII:C"
FT  Region          20..1667
FT                  /note= "heavy chain fragment"
FT  Modified-site   1327
FT                  /label= Phe, Giu, Pro
FT  Region          1668..2350
FT                  /note= "light chain fragment"
FT  Domain          760..1667
FT                  /note= "B domain"
XX
PN  WO9703195-A1.
XX
PD  30-JAN-1997.
XX
PF  09-JUL-1996;    96WO-US11444.
XX
PR  11-JUL-1995;    95US-0001025.
XX
PA  (CHIR ) CHIRON CORP.
XX
PI  Cohen FE,  Hung DT,  Innis M;
XX
DR  WPI; 1997-119050/11.
XX
PT  Factor VIII:C analog modified adjacent to a non-activating Arg
PT  residue - used in the treatment of haemophiliacs, by improvement of
PT  haemostasis
XX
PS  Claim 28; Page -; 90pp; English.
XX
CC  AAW11330-W11472 represent active Factor VIII:C analogues of the
CC  invention. These sequences were created by mutating the wild type Factor
CC  VIII:C coding sequence (see AA751357) using mutagenic primers. The
CC  analogues comprise a native Factor VIII:C polypeptide modified at a site
CC  adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC  dipeptide is created. Factor VIII:C is a large glycoprotein that
CC  participates in the blood coagulation cascade that ultimately converts
CC  soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC  deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC  X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC  activated by plasma proteases, such as thrombin. During activation the
CC  mature polypeptide is cleaved to generate heavy and light chain fragments
CC  that are further cleaved. Complexes of two or more of the analogues,
CC  nucleic acids and vectors encoding them may be used alone or in
CC  conjunction with each other, for the prevention or treatment of active
CC  Factor VIII:C deficiency in a mammal. The analogues may be used as
CC  immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC  improvement of haemostasis. The analogues are resistant to proteolytic
CC  cleavage and display increased plasma half-life. They may be administered
CC  at lower dosages and by different modes of administration.
XX
SQ  Sequence  2351 AA;

 Query Match             100.0%;  Score 12413;  DB 18;  Length 2351;
 Best Local Similarity   100.0%;  Pred. No. 0;
 Matches 2350;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDWVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDWVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEQQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Db       1141 QGPSPKQLVSLGPESVDQQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Db       1321 SQQNFVXQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Db       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAFSDV 1860

Db       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAFSDV 1860

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920

Db       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFHGH 1980

Db       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFHGH 1980

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Db       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Db       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Db       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Db       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351

Db       2341 EVLGCEAQDLY 2351


RESULT 12
AAW11419
ID   AAW11419 standard; Protein; 2351 AA.
XX
AC   AAW11419;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue, delta 1311, + Pro insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2351
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Misc-difference 1329..1330
FT                   /note= "site of 1 residue deletion"
FT   Modified-site   1330
FT                   /note= "inserted residue"
FT   Region          1668..2350
FT                   /note= "light chain fragment"
FT   Domain          760..1667
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11444.
XX
PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 27; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
```

```
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation of the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence    2351 AA;

  Query Match             100.0%;  Score 12413;  DB 18;  Length 2351;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2350;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 MQIELSTCPFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCPFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRPKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
```

```
Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
             ||||||||||| 
Db       2341 EVLGCEAQDLY 2351


RESULT 13
AAW11398
ID   AAW11398 standard; Protein; 2351 AA.
XX
AC   AAW11398;
XX
DT   18-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue, delta 746, + residue 746 insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2351
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Misc-difference 764..765
FT                   /note= "site of 1 residue deletion"
FT   Modified-site   765
FT                   /note= "inserted residue"
FT   Region          1668..2350
FT                   /note= "light chain fragment"
FT   Domain          760..1667
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX

PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11444.
XX
PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 23; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2351 AA;

  Query Match          100.0%;  Score 12413;  DB 18;  Length 2351;
  Best Local Similarity  100.0%;  Pred. No. 0;
  Matches 2350;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy         1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy        61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy       121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy       181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy       241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy       301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy       361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
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Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSHHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNPHHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHNSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHNSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEQGNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEQGNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYENKE 1380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYENKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
              ||||||||||| 
Db       2341 EVLGCEAQDLY 2351
```

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RESULT 14
AAW11387
ID   AAW11387 standard; Protein; 2351 AA.
XX
AC   AAW11387;
XX
DT   18-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue N357X.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
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KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2351
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Modified-site   376
FT                   /label= Phe, Glu, Pro
FT   Region          1668..2350
FT                   /note= "light chain fragment"
FT   Domain          760..1667
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US1444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 20; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2351 AA;

  Query Match             100.0%;  Score 12413;  DB 18;  Length 2351;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2350;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDXVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYTSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYTSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
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Qy       1201 LHENNTHNQEKKIQSEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 LHENNTHNQEKKIQSEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGATQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGATQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALLFTIFDETKSWYFTENMERNCRA 1920
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALLFTIFDETKSWYFTENMERNCRA 1920

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
             ||||||||||| 
Db       2341 EVLGCEAQDLY 2351


RESULT 15
AAW11362
ID   AAW11362 standard; Protein; 2351 AA.
XX
AC   AAW11362;
XX
DT   18-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue L277X.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2351
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Modified-site   296
FT                   /label= Phe, Glu, Pro
FT   Region          1668..2350
FT                   /note= "light chain fragment"
FT   Domain          760..1667
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 14; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
```

```
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2351 AA;

  Query Match          100.0%;  Score 12413;  DB 18;  Length 2351;
  Best Local Similarity  100.0%;  Pred. No. 0;
  Matches 2350;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 MQILELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQILELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKETQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKETQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKMTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy       1801 PYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 PYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
```

```
Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
                ||||||||||
Db       2341 EVLGCEAQDLY 2351


RESULT 16
AAP81113
ID   AAP81113 standard; protein; 2351 AA.
XX
AC   AAP81113;
XX
DT   08-OCT-1990  (first entry)
XX
DE   Factor VIII encoded by cDNA insert of pCLB89.
XX
KW   Factor VIII; blood clotting disorders.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Peptide          1..19
FT                    /label=signal sequence
FT
XX
PN   EP253455-A.
XX
PD   20-JAN-1988.
XX
PF   20-JUL-1987;  87EP-0201379.
XX
PR   18-JUL-1986;  86GB-0017594.
PR   03-DEC-1986;  86GB-0030699.
XX
PA   (KONN ) GIST-BROCADES NV.
XX
PI   Van Ooyen AJJ,  Andreoli PM,  Van Mourik JA,  Pannekoek H;
XX
DR   WPI; 1988-015822/03.
DR   NPSDB; N81439.
XX
PT   Expression system for producing factor VIII polypeptide in
PT   microbial cells - contg. open reading frame and functional
PT   initiation and termination regions.
XX
PS   Disclosure; ; 02pp; English.
XX
CC   Clone pCLB89 was produced by combining inserts from several
CC   positive clones isolated from a human liver  cDNA library.
CC   The DNA sequence can be inserted into expression vectors for
CC   the prodn. of the recombinant factor VIII.  The protein produced
CC   is useful for treating blood clotting disorders.
XX
SQ   Sequence   2351 AA;

  Query Match           100.0%;  Score 12412;  DB 9;  Length 2351;
  Best Local Similarity  100.0%;  Pred. No. 0;
  Matches 2350;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
```

RESULT 17
AAP80659
ID AAP80659 standard; protein; 2351 AA.
XX
AC AAP80659;
XX
DT 29-OCT-1990 (first entry)
XX
DE Sequence of human Factor VIII signal sequence and mature protein
DE encoded on plasmid pCLB89.
XX
KW Haemophilia A; bloodclotting; treatment; diagnosis.
XX
OS Homo sapiens.
XX
FH Key Location/Qualifiers
FT Peptide 1..19
FT /note="Signal peptide"
FT Protein 20..2351
XX
PN EP294910-A.
XX
PD 14-DEC-1988.
XX
PF 13-JUN-1988; 88EP-0201209.
XX
PR 12-JUN-1987; 87EP-0201121.
XX
PA (KONN) GIST-BROCADES NV.
XX
PI van Ooyen AJJ, Pannekoek H, Verbeet MP, van Leen RW;
XX
DR WPI; 1988-355361/50.
DR N-PSDB; AAN81096.
XX
PT Proteins having Factor VIII activity -
PT comprising deletion mutant proteins of Factor VIII in which
PT central region has been deleted
XX
PS Example; Fig 1; 37pp; English.
XX
CC The isolation of Factor VIII mRNA from human liver, and the preparation,
CC purification and identification of its cDNA and its assembly in
CC pBP121 resulting in plasmid pCLB89 have been described in patent
CC application EP 0253455. The Factor VIII polypetides of the invention
CC include deletion mutant proteins of Factor VIII in which all of central
CC region or "B domain" as well as a portion of the 92 kD region has been
CC deleted. The polypeptides have enhanced Factor VIII activity and/or
CC decreased immunogenicity and can be used for the treatment of
CC Haemophilia A. They can also be used to prepare antibodies. The Abs.

```
CC  can be used to determine the concn. of Factor VIII in a body fluid.
XX
SQ  Sequence   2351 AA;

  Query Match          100.0%;  Score 12412;  DB 9;  Length 2351;
  Best Local Similarity  100.0%;  Pred. No. 0;
  Matches 2350;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy        1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy       61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy      121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy      181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy      241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy      301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy      361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy      421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy      481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy      541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy      601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy      661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy      721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy      781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy      841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy      901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy      961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
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Db      961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy     1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy     1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy     1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy     1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy     1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy     1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy     1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy     1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy     1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy     1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy     1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy     1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHFIAAVERLWDYGMSSSPHVLRNR 1740
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHFIAAVERLWDYGMSSSPHVLRNR 1740

Qy     1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy     1801 PYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1801 PYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy     1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920

Qy     1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy     1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy     2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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```
Db       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 PPIIARYIRLHPTHYSIRSTLRMEWMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
              ||||||||||| 
Db       2341 EVLGCEAQDLY 2351


RESULT 18
AAW11437
ID   AAW11437 standard; Protein; 2351 AA.
XX
AC   AAW11437;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue, delta 1644, + Pro insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2351
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Misc-difference 1662..1663
FT                   /note= "site of 1 residue deletion"
FT   Modified-site   1663
FT                   /note= "inserted residue"
FT   Region          1668..2350
FT                   /note= "light chain fragment"
FT   Domain          760..1667
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 31; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence  2351 AA;

  Query Match             100.0%;  Score 12412;  DB 18;  Length 2351;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2350;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVPDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLPRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFTTIFDETKSWYFTENMERNCRA 1920
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFTTIFDETKSWYFTENMERNCRA 1920

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
              |||||||||||
Db       2341 EVLGCEAQDLY 2351

RESULT 19
AAW11427
ID   AAW11427 standard; Protein; 2351 AA.
XX
AC   AAW11427;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue, delta 1312, + Pro insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2351
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Misc-difference 1330..1331
FT                   /note= "site of 1 residue deletion"
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FT   Modified-site    1331
FT                    /note= "inserted residue"
FT   Region           1668..2350
FT                    /note= "light chain fragment"
FT   Domain           760..1667
FT                    /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;     96WO-US11444.
XX
PR   11-JUL-1995;     95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 29; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51257) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence  2351 AA;

  Query Match             100.0%;  Score 12412;  DB 18;  Length 2351;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2350;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESAKWIQRTHGKNSLNSG 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESAKWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSPRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
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Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
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Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
             ||||||||||| 
Db       2341 EVLGCEAQDLY 2351


RESULT 20
AAW11408
ID   AAW11408 standard; Protein; 2351 AA.
XX
```

```
AC   AAW11408;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue, delta 777, + residue 777 insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2351
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Misc-difference 795..796
FT                   /note= "site of 1 residue deletion"
FT   Modified-site   796
FT                   /note= "inserted residue, optionally deleted"
FT   Region          1668..2350
FT                   /note= "light chain fragment"
FT   Domain          760..1667
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 25; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2351 AA;
```

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Query Match          100.0%;  Score 12412;  DB 18;  Length 2351;
Best Local Similarity  100.0%;  Pred. No. 0;
Matches 2350;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy        1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy       61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy      121 GVSYWKASEGAETDDQTSQRKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      121 GVSYWKASEGAETDDQTSQRKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy      181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy      241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy      301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy      361 EAEDYDDDLDTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      361 EAEDYDDDLDTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy      421 PDDRSYKSQYLNNGPQRIGKKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      421 PDDRSYKSQYLNNGPQRIGKKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy      481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy      541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy      601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy      661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDPRNRG 720
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDPRNRG 720

Qy      721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy      781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      781 PENDIEKTDPWFAHRPPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy      841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy      901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy      961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy     1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy     1081 NHMSNKTTSSKNMEMVQQKKESGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy     1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEPTKDVGLKEMVFPSSRNLFLTNLDN 1200
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEPTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy     1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy     1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy     1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy     1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy     1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy     1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy     1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy     1621 NACESNHAIAAINEQGNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1621 NACESNHAIAAINEQGNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy     1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy     1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy     1801 PYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1801 PYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy     1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCRA 1920
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCRA 1920

Qy     1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy     1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy     2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy     2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
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Db       2101 HGIKTQGARQKPSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
              ||||||||||
Db       2341 EVLGCEAQDLY 2351


RESULT 21
AAW11347
ID   AAW11347 standard; Protein; 2351 AA.
XX
AC   AAW11347;
XX
DT   17-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue K251P.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2351
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Modified-site   270
FT                   /label= K251P
FT   Region          1668..2350
FT                   /note= "light chain fragment"
FT   Domain          760..1667
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11444.
XX
PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE, Hung DT, Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 11; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2351 AA;

  Query Match             100.0%;  Score 12412;  DB 18;  Length 2351;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2350;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
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Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
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Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
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Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLESSGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLESSGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
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Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFPESARWIQRTHGKNSLNSG 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEQGNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFTNLDN 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEQGNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFTNLDN 1200

Qy       1201 LHENNYHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
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Db       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy       1801 PYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
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Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALLFTIFDETKSWYFTENMERNCRA 1920
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Db       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALLFTIFDETKSWYFTENMERNCRA 1920

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
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Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
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Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
              |||||||||||
Db       2341 EVLGCEAQDLY 2351


RESULT 22
AAW11332
ID   AAW11332 standard; Protein; 2351 AA.
XX
AC   AAW11332;
XX
DT   17-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue Q218X.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2351
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Modified-site   237
FT                   /label= Phe, Glu, Pro
FT   Region          1668..2350
FT                   /note= "light chain fragment"
FT   Domain          760..1667
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
```

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XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US1144.
XX
PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE, Hung DT, Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 8; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence  2351 AA;
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  Query Match          100.0%;  Score 12412;  DB 18;  Length 2351;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2350;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
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Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMXDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPTNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDNVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDNVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
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Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy.      2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
              |||||||||||
Db       2341 EVLGCEAQDLY 2351
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RESULT 23
AAW11396
ID   AAW11396 standard; Protein; 2351 AA.
XX
AC   AAW11396;
XX
DT   18-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue D560X.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2351
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Modified-site   579
FT                   /label= Phe, Glu, Pro
FT   Region          1668..2350
FT                   /note= "light chain fragment"
FT   Domain          760..1667
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11444.
XX
PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 22; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2351 AA;

  Query Match             99.9%;  Score 12411;  DB 18;  Length 2351;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2350;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db        61 TSVVYKKTLFVEFTDHLFNIAKPRPPWWGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy       121 GVSVWKASEGAEYDDQTSQREKEDDKVPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Db       121 GVSVWKASEGAEYDDQTSQREKEDDKVPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy       181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Db       181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy       241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVICGMGTTPEVHSIFLEGHTFLVRNH 300

Db       241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVICGMGTTPEVHSIFLEGHTFLVRNH 300

Qy       301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Db       301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy       361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Db       361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy       421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Db       421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy       481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Db       481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy       541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Db       541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVXQRGNQIMSDKRNVILFSVFDE 600

Qy       601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Db       601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy       661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Db       661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy       721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Db       721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy       781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Db       781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy       841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Db       841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy       901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Db       901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy       961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Db       961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy      1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Db      1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy      1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Db      1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy      1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Db      1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy      1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Db      1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy      1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Db      1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy      1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Db      1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy      1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Db      1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy      1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEWTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Db      1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEWTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy      1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Db      1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy      1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Db      1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy      1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Db      1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy      1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Db      1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy      1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Db      1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy      1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Db      1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy      1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCRA 1920

Db      1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCRA 1920

Qy      1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Db      1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy      1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Db      1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy      2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Db      2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy      2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Db      2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy      2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSFTKMFA 2220

Db      2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSFTKMFA 2220

Qy      2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Db      2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
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Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQ!ALRM 2340

Qy       2341 EVLGCEAQDLY 2351
             ||||||||||| 
Db       2341 EVLGCEAQDLY 2351


RESULT 24
AAW11371
ID   AAW11371 standard; Protein; 2351 AA.
XX
AC   AAW11371;
XX
DT   18-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue N280X.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2351
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Modified-site   299
FT                   /label= Phe, Glu, Pro
FT   Region          1668..2350
FT                   /note= "light chain fragment"
FT   Domain          760..1667
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11444.
XX
PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 16; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2351 AA;

  Query Match             99.9%;  Score 12411;  DB 18;  Length 2351;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2350;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy         1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy        61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy       121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy       181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy       241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRXH 300

Qy       301 RQASLETSRITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy       361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy       421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy       481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy       541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy       601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy       661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy       721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy       781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy       841 PCAIDSNNSLSEMTHFRPQLHHSGDWVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDWVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFIQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy       1801 PYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 PYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
              ||||||||||.
Db       2341 EVLGCEAQDLY 2351


RESULT 25
AAW00465
ID   AAW00465 standard; Protein; 2351 AA.
XX
AC   AAW00465;
XX
DT   19-SEP-1996  (first entry)
XX
DE   Factor-VIII.
XX
KW   Factor-VIII; retrovirus; vector; haemophilia A; gene therapy.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /label= Sig_peptide
FT   Protein         20..2351
FT                   /label= Mat_protein
XX
PN   WO9621035-A2.
XX
PD   11-JUL-1996.
XX
PF   18-DEC-1995;    95WO-US16582.
XX
PR   30-DEC-1994;    94US-0366851.
XX
PA   (CHIR ) CHIRON VIAGENE INC.
XX
PI   Bodner M,  Chang S,  Chi-Tang Hsu D,  De Polo NJ;
XX
DR   WPI; 1996-334010/33.
DR   N-PSDB; AAT31031.
XX
PT   Retroviral vector directing expression of full length factor VIII -
PT   used in the gene therapy and treatment of haemophilia A
XX
PS   Disclosure; Page 69-75; 86pp; English.
XX
CC   A full-length cDNA clone (AAT31031) codes for human Factor-VIII
CC   (AAW00465). a trace plasma glycoprotein which acts as a cofactor in
CC   conjunction with Factor-IXa in the activation of Factor-X.
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CC   Retroviral vectors comprising the full-length cDNA can be efficiently
CC   packaged into infectious retroviral particles.  These may be used to
CC   transduce cells either in vivo or ex vivo.  Factor-VIII expressed
CC   from such transduced cells will be processed and transported in a
CC   fashion analogous to the expression product of a normal Factor-VIII
CC   gene.  Retroviral particles harbouring such vectors will be useful
CC   in the gene therapy of haemophilia A.
XX
SQ   Sequence   2351 AA;

     Query Match             99.9%;  Score 12409;  DB 17;  Length 2351;
     Best Local Similarity   100.0%;  Pred. No. 0;
     Matches 2350;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQRSEKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQRSEKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHRSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy       1801 PYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 PYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
```

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Qy       1981 VPTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 VPTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSPTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSPTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
              |||||||||||
Db       2341 EVLGCEAQDLY 2351


RESULT 26
AAW11454
ID   AAW11454 standard; Protein; 2351 AA.
XX
AC   AAW11454;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue H1646Y.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2351
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Modified-site   1665
FT                   /label= Phe, Glu, Pro
FT   Region          1668..2350
FT                   /note= "light chain fragment"
FT   Domain          760..1667
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 34; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence  2351 AA;

  Query Match             99.9%;  Score 12409;  DB 18;  Length 2351;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2350;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy         1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy        61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy       121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy       181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy       241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy       301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy       361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy       421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy       481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy       541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDPKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDPKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy        1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy        1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy        1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy        1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy        1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy        1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy        1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy        1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy        1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy        1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy        1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy        1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy        1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy        1801 PYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1801 PYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy        1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALLFTIFDETKSWYFTENMERNCRA 1920
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALLFTIFDETKSWYFTENMERNCRA 1920

Qy        1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy        1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy        2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy        2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy        2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy        2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy        2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy        2341 EVLGCEAQDLY 2351
               ||||||||||| 
Db        2341 EVLGCEAQDLY 2351

RESULT 27
AAB48843
ID   AAB48843 standard; protein; 2351 AA.
XX
AC   AAB48843;
XX
DT   13-MAR-2001 (first entry)
XX
DE   Human factor VIII, SEQ ID NO:2.
XX
KW   Factor VIII; human; A2 domain; C2 domain; LRP-mediated plasma clearance;
KW   receptor-dependent clearance; receptor-independent clearance;
KW   haemophilia; half-life.
XX
OS   Homo sapiens.
XX
PN   WO200071714-A2.
XX
PD   30-NOV-2000.
XX
PF   24-MAY-2000; 2000WO-US14111.
XX
PR   24-MAY-1999;  99US-0135847.
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XX
PA   (AMNA-) AMERICAN NAT RED CROSS.
XX
PT   Saenko EL,  Strickland DK;
XX
DR   WPI; 2001-025163/03.
DR   N-PSDB; AAC87526.
XX
PT   Factor VIII mutants having increased half-life useful for treating
PT   hemophilia, comprise one or more amino acid substitutions in the A2
PT   and/or C2 domain of factor VIII  -
XX
PS   Disclosure; Fig 3A-B; 121pp; English.
XX
CC   The invention relates to human factor VIII mutants comprising an amino
CC   acid substitution at one or more positions in the A2 domain and/or an
CC   amino acid substitution at one or more positions in the C2 domain.
CC   The invention also encompasses a factor VIII mutant which lacks a B
CC   domain (AAB48842). The factor VIII mutants have an increased half-life
CC   in the bloodstream. The A2 domain mutants exhibit reduced LRP-dependent
CC   (receptor-dependent) clearance of factor VIII, while C2 domain mutants
CC   have reduced receptor-independent clearance. The invention also relates
CC   to a method of using RAP (receptor associated protein), a protein which
CC   inhibits LRP (low density lipoprotein related protein)-mediated ligand
CC   internalisation, to increase the half-life of factor VIII. The mutant
CC   factor VIII proteins, and nucleotides encoding them, are useful
CC   for treating haemophilia. RAP, LRP-binding RAP mutants or fragments, and
CC   nucleic acids encoding them may also be used in the treatment of
CC   haemophilia, in combination with a mutant factor VIII protein or DNA of
CC   the invention. The invention provides means of increasing the half-life
CC   of factor VIII by reducing its clearance from plasma. The present
CC   sequence represents human factor VIII.
XX
SQ   Sequence  2351 AA;

  Query Match          99.9%;  Score 12609;  DB 22;  Length 2351;
  Best Local Similarity  100.0%;  Pred. No. 0;
  Matches 2350;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy        1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy       61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy      121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy      181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy      241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy      301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy      361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy      421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy      481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy      541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy      601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy      661 IGAQTDFLSVFFSGYTFKHKMVFEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      661 IGAQTDFLSVFFSGYTFKHKMVFEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy      721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHRSTRQKQFNATTI 780

Qy      781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy      841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy      901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy      961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSILSLKTN 1020
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSILSLKTN 1020

Qy     1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy     1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy     1141 QGPSPKQLVSLGPEKSVEQQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1141 QGPSPKQLVSLGPEKSVEQQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy     1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy     1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy     1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy     1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy     1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy     1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy     1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
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Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
             ||||||||||| 
Db       2341 EVLGCEAQDLY 2351


RESULT 28
AAW11399
ID   AAW11399 standard; Protein; 2351 AA.
XX
AC   AAW11399;
XX
DT   18-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue, delta 748, + residue 748 insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide          1..19
FT                    /note= "signal peptide"
FT   Protein          20..2351
FT                    /note= "mature Factor VIII:C"
FT   Region           20..1667
FT                    /note= "heavy chain fragment"
FT   Misc-difference  766..767
FT                    /note= "site of 1 residue deletion"
FT   Modified-site    767
FT                    /note= "inserted residue, optionally deleted"
FT   Region           1668..2350
FT                    /note= "light chain fragment"
FT   Domain           760..1667
FT                    /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 23; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjuction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different routes of administration.
XX
SQ   Sequence   2351 AA;

  Query Match          99.9%;  Score 12408;  DB 18;  Length 2351;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2350;  Conservative    0;  Mismatches   .1;  Indels    0;  Gaps    0;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
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Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAIYVKVDSCPEEPQLRMKNNE 360
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAIYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLFDSEMDVVRFPDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLFDSEMDVVRFPDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQPNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQPNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEWTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEWTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEQPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKKEQPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEQQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEQQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLDNQTKQIVEKYACTTRISPNT 1320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLDNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTESNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTESNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
```

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                     ||||||||||
Db          2341 EVLGCEAQDLY 2351


RESULT 29
AAW11404
ID   AAW11404 standard; Protein; 2351 AA.
XX
AC   AAW11404;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue, delta 746, + residue 745 insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2351
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Modified-site   764
FT                   /label= Phe, Glu, Pro
FT                   /note= "inserted residue"
FT   Misc-difference 765..766
FT                   /note= "site of 1 residue deletion"
FT   Region          1668..2350
FT                   /note= "light chain fragment"
FT   Domain          760..1667
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 24; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence  2351 AA;

  Query Match             99.9%;  Score 12408;  DB 18;  Length 2351;
  Best Local Similarity   99.9%;  Pred. No. 0;
  Matches 2349;  Conservative    1;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 MQIELSTCFFLCLLRFCSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKETQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKETQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQXNRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
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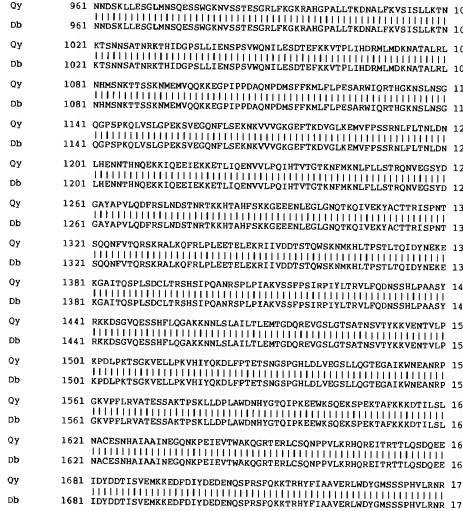

RESULT 30
AAW11456
ID AAW11456 standard; Protein; 2352 AA.
XX
AC AAW11456;
XX
DT 20-NOV-1997 (first entry)
XX
DE Active Factor VIII:C analogue residue 1719 P insertion.
XX
KW Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW proteolytic cleavage.
XX
OS Homo sapiens.
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Peptide 1..19
FT /note= "signal peptide"
FT Protein 20..2352
FT /note= "mature Factor VIII:C"
FT Region 20..1667
FT /note= "heavy chain fragment"
FT Region 1668..2351
FT /note= "light chain fragment"
FT Domain 760..1667
FT /note= "B domain"
FT Misc-difference 1738
FT /note= "inserted residue"
XX
PN WO9703195-A1.
XX
PD 30-JAN-1997.
XX
PF 09-JUL-1996; 96WO-US11444.
XX
PR 11-JUL-1995; 95US-0001025.
XX
PA (CHIR) CHIRON CORP.
XX
PI Cohen FE, Hung DT, Innis M;
XX
DR WPI; 1997-119050/11.

XX
PT Factor VIII:C analog modified adjacent to a non-activating Arg
PT residue - used in the treatment of haemophiliacs, by improvement of
PT haemostasis
XX
PS Claim 35; Page -; 90pp; English.
XX
CC AAW11330-W11472 represent active Factor VIII:C analogues of the
CC invention. These sequences were created by mutating the wild type Factor
CC VIII:C coding sequence (see AAY51357) using mutagenic primers. The
CC analogues comprise a native Factor VIII:C polypeptide modified at a site
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC dipeptide is created. Factor VIII:C is a large glycoprotein that
CC participates in the blood coagulation cascade that ultimately converts
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC activated by plasma proteases, such as thrombin. During activation the
CC mature polypeptide is cleaved to generate heavy and light chain fragments
CC that are further cleaved. Complexes of two or more of the analogues,
CC nucleic acids and vectors encoding them may be used alone or in
CC conjunction with each other, for the prevention or treatment of active
CC Factor VIII:C deficiency in a mammal. The analogues may be used as
CC immunogens raise antibodies, and in the treatment of haemophiliacs, by
CC improvement of haemostasis. The analogues are resistant to proteolytic
CC cleavage and display increased plasma half-life. They may be administered
CC at lower dosages and by different modes of administration.
XX
SQ Sequence 2352 AA;

Query Match 99.9%; Score 12407.5; DB 18; Length 2352;
Best Local Similarity 100.0%; Pred. No. 0;
Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;

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Qy       1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy      61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy     121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy     181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy     241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy     301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy     361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy     421 PDDRSTKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     421 PDDRSTKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy     481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy     541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy     601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy     661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy     721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy     781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy     841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy     901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy     961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy    1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy    1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy    1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy    1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy    1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy    1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy    1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy    1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy    1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy    1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy    1621 NACESNNAIAAINEQGNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1621 NACESNNAIAAINEQGNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
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Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVL-RN 1739
                                                                          ||
Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLPRN 1740

Qy       1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy       1800 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy       1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy       1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy       1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy       2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy       2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy       2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy       2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy       2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy       2340 MEVLGCEAQDLY 2351
              ||||||||||||
Db       2341 MEVLGCEAQDLY 2352


RESULT 31
AAW11458
ID   AAW11458 standard; Protein; 2352 AA.
XX
AC   AAW11458;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 1720 P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Region          1668..2351
FT                   /note= "light chain fragment"
FT   Domain          760..1667
FT                   /note= "B domain"
FT   Misc-difference 1739
FT                   /note= "inserted residue"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE, Hung DT, Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 35; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2352 AA;

  Query Match          99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity  100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy         1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy        61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy       121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy       181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy       241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db        241 AASARAWPKMHTVNGTVNRSLPGLIGCHRKSVYHWIVGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RSGWSLISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAVFKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAVFKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEQGNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLPLTNLDN 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEQGNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLPLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVDDTSTQWSKMKHLTPSTLTQIDYNEKE 1380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVDDTSTQWSKMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQITPKEEWKSQEKSPEKTAFKKKDTILSL 1620
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQITPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN- 1739
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||| |
Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNP 1740

Qy       1740 RAQSGSVPQFKKVVPQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||| |
Db       1741 RAQSGSVPQFKKVVPQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy       1800 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||| |
Db       1801 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy       1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCR 1919
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||| |
Db       1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCR 1920

Qy       1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||| |
Db       1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy       1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||| |
Db       1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy       2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||| |
Db       2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy       2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||| |
Db       2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy       2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNWF 2219
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||| |
Db       2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNWF 2220

Qy       2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||| |
Db       2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy       2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSPTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||| |
Db       2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSPTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy       2340 MEVLGCEAQDLY 2351
              ||||||||||||
Db       2341 MEVLGCEAQDLY 2352

RESULT 32
AAW11459
ID   AAW11459 standard; Protein; 2352 AA.
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XX
AC   AAW11459;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 1718 F/E/P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Region          1668..2351
FT                   /note= "light chain fragment"
FT   Domain          760..1667
FT                   /note= "B domain"
FT   Modified-site   1737
FT                   /label= Phe, Glu, Pro
FT                   /note= "inserted residue"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 36; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAY51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2352 AA;
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 Query Match          99.9%;  Score 12407.5;  DB 18;  Length 2352;
 Best Local Similarity   100.0%;  Pred. No. 0;
 Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDWVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDWVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
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Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Db       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHV-LRN 1739

Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVXLRN 1740

Qy       1740 RAQGSSVFQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799

Db       1741 RAQGSSVFQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy       1800 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859

Db       1801 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy       1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919

Db       1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy       1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979

Db       1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy       1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039

Db       1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy       2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099

Db       2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy       2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159

Db       2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy       2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219

Db       2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy       2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279

Db       2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy       2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSPTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339

Db       2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSPTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy       2340 MEVLGCEAQDLY 2351

Db       2341 MEVLGCEAQDLY 2352


RESULT 33
AAW11463
ID   AAW11463 standard; Protein; 2352 AA.
XX
AC   AAW11463;
XX
DT   21-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 1721 P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Region          1668..2351
FT                   /note= "light chain fragment"
FT   Domain          760..1667
FT                   /note= "B domain"
FT   Misc-difference 1740
FT                   /note= "inserted residue"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 37; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
```

```
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence    2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN- 1739
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNP 1740

Qy       1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy       1800 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
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                     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1801 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy        1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCR 1919
                     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCR 1920

Qy        1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
                     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy        1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
                     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy        2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
                     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy        2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
                     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy        2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
                     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy        2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
                     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy        2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSPTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
                     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSPTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy        2340 MEVLGCEAQDLY 2351
                     ||||||||||||
Db        2341 MEVLGCEAQDLY 2352


RESULT 34
AAW11464
ID    AAW11464 standard; Protein; 2352 AA.
XX
AC    AAW11464;
XX
DT    21-NOV-1997  (first entry)
XX
DE    Active Factor VIII:C analogue residue 1722 P insertion.
XX
KW    Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW    fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW    plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW    proteolytic cleavage.
XX
OS    Homo sapiens.
OS    Synthetic.
XX
FH    Key             Location/Qualifiers
FT    Peptide         1..19
FT                    /note= "signal peptide"
FT    Protein         20..2352
FT                    /note= "mature Factor VIII:C"
FT    Region          20..1667
FT                    /note= "heavy chain fragment"
FT    Region          1668..2351
FT                    /note= "light chain fragment"
FT    Domain          760..1667
FT                    /note= "B domain"
FT    Misc-difference 1741
FT                    /note= "inserted residue"
XX
PN    WO9703195-A1.
XX
PD    30-JAN-1997.
XX
PF    09-JUL-1996;    96WO-US11444.
XX
PR    11-JUL-1995;    95US-0001025.
XX
PA    (CHIR ) CHIRON CORP.
XX
PI    Cohen PE,  Hung DT,  Innis M;
XX
DR    WPI; 1997-119050/11.
XX
PT    Factor VIII:C analog modified adjacent to a non-activating Arg
PT    residue - used in the treatment of haemophiliacs, by improvement of
PT    haemostasis
XX
PS    Claim 37; Page -; 90pp; English.
XX
CC    AAW11330-W11472 represent active Factor VIII:C analogues of the
CC    invention. These sequences were created by mutating the wild type Factor
CC    VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC    analogues comprise a native Factor VIII:C polypeptide modified at a site
CC    adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC    dipeptide is created. Factor VIII:C is a large glycoprotein that
CC    participates in the blood coagulation cascade that ultimately converts
CC    soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC    deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC    X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC    activated by plasma proteases, such as thrombin. During activation the
CC    mature polypeptide is cleaved to generate heavy and light chain fragments
CC    that are further cleaved. Complexes of two or more of the analogues,
CC    nucleic acids and vectors encoding them may be used alone or in
CC    conjunction with each other, for the prevention or treatment of active
CC    Factor VIII:C deficiency in a mammal. The analogues may be used as
CC    immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC    improvement of haemostasis. The analogues are resistant to proteolytic
CC    cleavage and display increased plasma half-life. They may be administered
CC    at lower dosages and by different modes of administration.
XX
SQ    Sequence   2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
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Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVVSSDDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVVSSDDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEWTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEWTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQTHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQTHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy       1741 -AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 PAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy       1800 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy       1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy       1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy       1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy       2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy       2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy       2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy       2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy       2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy       2340 MEVLGCEAQDLY 2351
              ||||||||||||
Db       2341 MEVLGCEAQDLY 2352

RESULT 35
AAW11438
ID   AAW11438 standard; Protein; 2352 AA.
XX
AC   AAW11438;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 1645 P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
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```
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Misc-difference 1664
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          760..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE, Hung DT, Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 31; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophilacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQILELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQILELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKETQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKETQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
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Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDWVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDWVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
```

```
Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLPQDNSSHLPAASY 1440
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLPQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLK-RHQREITRTTLQSDQE 1679
             ||||||||||||||||||||||||||||||||||||||||||| |||||||||||||||||
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKPRHQREITRTTLQSDQE 1680

Qy       1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy       1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy       1800 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy       1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCR 1919
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCR 1920

Qy       1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy       1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy       2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy       2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy       2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy       2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy       2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy       2340 MEVLGCEAQDLY 2351
             ||||||||||||
Db       2341 MEVLGCEAQDLY 2352
```

RESULT 36
AAW11439
ID AAW11439 standard; Protein; 2352 AA.
XX
AC AAW11439;
XX
DT 20-NOV-1997 (first entry)
XX
DE Active Factor VIII:C analogue residue 1646 P insertion.
XX
KW Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW proteolytic cleavage.
XX
OS Homo sapiens.
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Peptide 1..19
FT /note= "signal peptide"
FT Protein 20..2352
FT /note= "mature Factor VIII:C"
FT Region 20..1668
FT /note= "heavy chain fragment"
FT Misc-difference 1665
FT /note= "inserted residue"
FT Region 1669..2351
FT /note= "light chain fragment"
FT Domain 760..1668
FT /note= "B domain"
XX
PN WO9703195-A1.
XX
PD 30-JAN-1997.
XX
PF 09-JUL-1996; 96WO-US11444.
XX
PR 11-JUL-1995; 95US-0001025.
XX
PA (CHIR) CHIRON CORP.
XX
PI Cohen FE, Hung DT, Innis M;
XX
DR WPI; 1997-119050/11.
XX
PT Factor VIII:C analog modified adjacent to a non-activating Arg
PT residue - used in the treatment of haemophiliacs, by improvement of
PT haemostasis
XX
PS Claim 31; Page -; 90pp; English.
XX
CC AAW11330-W11472 represent active Factor VIII:C analogues of the
CC invention. These sequences were created by mutating the wild type Factor
CC VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC analogues comprise a native Factor VIII:C polypeptide modified at a site
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC dipeptide is created. Factor VIII:C is a large glycoprotein that
CC participates in the blood coagulation cascade that ultimately converts
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC activated by plasma proteases, such as thrombin. During activation the
CC mature polypeptide is cleaved to generate heavy and light chain fragments

CC that are further cleaved. Complexes of two or more of the analogues,
CC nucleic acids and vectors encoding them may be used alone or in
CC conjunction with each other, for the prevention or treatment of active
CC Factor VIII:C deficiency in a mammal. The analogues may be used as
CC immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC improvement of haemostasis. The analogues are resistant to proteolytic
CC cleavage and display increased plasma half-life. They may be administered
CC at lower dosages and by different modes of administration.
XX
SQ Sequence 2352 AA;

Query Match 99.9%; Score 12407.5; DB 18; Length 2352;
Best Local Similarity 100.0%; Pred. No. 0;
Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;

```
Qy       1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy      61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy     121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy     181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy     241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy     301 RQASLEISPSTFLTAQTTLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     301 RQASLEISPSTFLTAQTTLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy     361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy     421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy     481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy     541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy     601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy     661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy     721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy     781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy     841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy     901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy     961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy    1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy    1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy    1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy    1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy    1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy    1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy    1381 KGATTQSPSLDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1381 KGATTQSPSLDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy    1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy    1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy    1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy    1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKR-HQREITRTTLQSDQE 1679
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRPHQREITRTTLQSDQE 1680

Qy    1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy    1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy    1800 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWYFSD 1859
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1801 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWYFSD 1860

Qy    1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy    1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980
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Qy       1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy       2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy       2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy       2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy       2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy       2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSPTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSPTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy       2340 MEVLGCEAQDLY 2351
             ||||||||||||
Db       2341 MEVLGCEAQDLY 2352


RESULT 37
AAW11442
ID   AAW11442 standard; Protein; 2352 AA.
XX
AC   AAW11442;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 1644 F/E/P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Modified-site   1663
FT                   /label= Phe, Glu, Pro
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          760..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX

PI   Cohen PE, Hung DT, Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 32; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
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Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEQGNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEQGNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVL-KRHQREITRTTLQSDQE 1679
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Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLXRHQREITRTTLQSDQE 1680

Qy       1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy       1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy       1800 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy       1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy       1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy       1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy       2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy       2100 IHGIKTQGAHQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 IHGIKTQGAHQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy       2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy       2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy       2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy       2340 MEVLGCEAQDLY 2351
              ||||||||||||
Db       2341 MEVLGCEAQDLY 2352

RESULT 38
AAW11447
ID   AAW11447 standard; Protein; 2352 AA.
XX
AC   AAW11447;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 1648 P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
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```
FT   Protein           20..2352
FT                     /note= "mature Factor VIII:C"
FT   Region            20..1668
FT                     /note= "heavy chain fragment"
FT   Misc-difference   1667
FT                     /note= "inserted residue"
FT   Region            1669..2351
FT                     /note= "light chain fragment"
FT   Domain            760..1668
FT                     /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11444.
XX
PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen PE, Hung DT, Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 33; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2352 AA;
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```
  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEQQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEQQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
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Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
             .  ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKDTILSL 1620
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQ-REITRTTLQSDQE 1679
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQPREITRTTLQSDQE 1680

Qy       1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy       1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy       1800 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy       1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy       1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy       1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy       2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy       2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy       2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy       2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy       2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSPTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSPTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy       2340 MEVLGCEAQDLY 2351
             ||||||||||||
Db       2341 MEVLGCEAQDLY 2352
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RESULT 39
AAW11450
ID   AAW11450 standard; Protein; 2352 AA.
XX
AC   AAW11450;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 1649 P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Misc-difference 1668
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          760..1667
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 33; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
```

```
SQ   Sequence   2352 AA;

  Query Match          99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity  100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy       1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy      61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy     121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy     181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy     241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVICGMGTTPEVHSIFLEGHTFLVRNH 300
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVICGMGTTPEVHSIFLEGHTFLVRNH 300

Qy     301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy     361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy     421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy     481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy     541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy     601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy     661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy     721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy     781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy     841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy     901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy     961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy    1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy    1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy    1141 QGPSPKQLVSLGPEKSVEQQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1141 QGPSPKQLVSLGPEKSVEQQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy    1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy    1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy    1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy    1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy    1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy    1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy    1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy    1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQR-EITKTTLQSDQE 1679
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQRPEITKTTLQSDQE 1680

Qy    1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy    1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy    1800 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1801 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy    1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy    1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy    1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy    2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100
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Qy        2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy        2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy        2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy        2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy        2340 MEVLGCEAQDLY 2351
               ||||||||||||
Db        2341 MEVLGCEAQDLY 2352


RESULT 40
AAW11451
ID   AAW11451 standard; Protein; 2352 AA.
XX
AC   AAW11451;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 1647 F/E/P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Modified-site   1666
FT                   /label= Phe, Glu, Pro
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          760..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE, Hung DT, Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 34; Page -; 90pp; English.
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XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AA751357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence  2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
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Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEXSVEGQNFLSEKNKVVVGKGEPTKDVGLKEMVFPSSRNLFLTNLDN 1200

Db       1141 QGPSPKQLVSLGPEXSVEGQNFLSEKNKVVVGKGEPTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEISKKETLIQENVVLPQIHTVTGTKNPMKNLFLLSTRQNVEGSYD 1260

Db       1201 LHENNTHNQEKKIQEEISKKETLIQENVVLPQIHTVTGTKNPMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKDTILSL 1620

Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKDTILSL 1620

Qy       1621 NACESNHAIAAINEQGNKPEIEVTWAKQGRTERLCSQNPPVLKRH-QREITRTTLQSDQE 1679

Db       1621 NACESNHAIAAINEQGNKPEIEVTWAKQGRTERLCSQNPPVLKRHXQREITRTTLQSDQE 1680

Qy       1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739

Db       1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy       1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799

Db       1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy       1800 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859

Db       1801 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy       1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919

Db       1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy       1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979

Db       1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy       1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039

Db       1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy       2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099

Db       2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy       2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159

Db       2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy       2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219

Db       2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy       2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279

Db       2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy       2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339

Db       2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy       2340 MEVLGCEAQDLY 2351

Db       2341 MEVLGCEAQDLY 2352

RESULT 41
AAW11423
ID   AAW11423 standard; Protein; 2352 AA.
XX
AC   AAW11423;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 1309 F/E/P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Modified-site   1328
FT                   /label= Phe, Glu, Pro
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
```

```
FT   Domain            760..1668
FT                     /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;      96WO-US1144.
XX
PR   11-JUL-1995;      95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 28; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGKKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGKKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVT-QRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
              |||||| |||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTXQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy       1380 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440
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Qy       1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500

Qy       1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANH 1559
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy       1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1619
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1620

Qy       1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1679
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1680

Qy       1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy       1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy       1800 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy       1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy       1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy       1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy       2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy       2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy       2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy       2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy       2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy       2340 MEVLGCEAQDLY 2351
             ||||||||||||
Db       2341 MEVLGCEAQDLY 2352


RESULT 42
AAW11426
ID   AAW11426 standard; Protein; 2352 AA.
XX
AC   AAW11426;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 1313 P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Misc-difference 1332
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          760..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 29; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAP51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence  2352 AA;

  Query Match          99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity  100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy         1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHKKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHKKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLNNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLNNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEQGNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEQGNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSK-RALKQFRLPLEETELEKRIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
              ||||||||||| |||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKPRALKQFRLPLEETELEKRIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy       1380 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440

Qy       1440 YRKKDSGVQESSHFLQSAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 YRKKDSGVQESSHFLQSAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500

Qy       1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy       1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTIL 1619
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTIL 1620

Qy       1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1679
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1680

Qy       1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy       1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy       1800 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy       1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCR 1919
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCR 1920

Qy       1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy       1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy       2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy       2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy       2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220
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Qy       2220 ATWSPSRARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 ATWSPSRARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy       2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy       2340 MEVLGCEAQDLY 2351
             ||||||||||||
Db       2341 MEVLGCEAQDLY 2352


RESULT 43
AAW11429
ID   AAW11429 standard; Protein; 2352 AA.
XX
AC   AAW11429;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 1314 P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Misc-difference 1335
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          760..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 29; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy         1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy        61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy       121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy       181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy       241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy       301 RQASLSISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
             |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy       361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy       421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy       481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy       541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy       601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy       661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy       721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy       781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db        781 PENDIEKTDPWPAHRTPWPKIQNVSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy        1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy        1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFKMLFLPESARWIQRTHGKNSLNSG 1140
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy        1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFTNLDN 1200
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFTNLDN 1200

Qy        1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy        1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy        1321 SQQNFVTQRSKR-ALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
               |||||||||||| |||||||||||||||||||||||||||||||||||||||||||||||
Db        1321 SQQNFVTQRSKRPALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy        1380 EKGATQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1381 EKGATQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440

Qy        1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500

Qy        1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy        1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1619
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1620

Qy        1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1679
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1680

Qy        1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy        1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy        1800 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1801 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy        1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy        1920 APCNIQMDDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1921 APCNIQMDDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy        1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy        2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy        2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy        2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy        2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy        2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy        2340 MEVLGCEAQDLY 2351
               ||||||||||||
Db        2341 MEVLGCEAQDLY 2352


RESULT 44
AAW11433
ID   AAW11433 standard; Protein; 2352 AA.
XX
AC   AAW11433;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 1312 F/E/P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Modified-site   1331
FT                   /label= Phe, Glu, Pro
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          760..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11444.
XX
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PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 30; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analoques of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analoques comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   Soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analoques,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analoques may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analoques are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence  2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy       1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy      61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy     121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy     181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy     241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy     301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy     361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy     421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy     481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy     541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy     601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy     661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy     721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy     781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy     841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy     901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy     961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy    1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy    1081 NHMSNKTTSSKNMEMVQQKEGPIPPDAQNPDMSFKMLFLPESARWIQRTHGKNSLNSG 1140
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1081 NHMSNKTTSSKNMEMVQQKEGPIPPDAQNPDMSFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy    1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy    1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy    1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy    1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy    1380 EKGAITQSPLSDCLTRSHSIPQAWRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1381 EKGAITQSPLSDCLTRSHSIPQAWRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440

Qy    1440 YRKKDSGVQESSHFLQGAKKNNLSLAIITLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1441 YRKKDSGVQESSHFLQGAKKNNLSLAIITLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500

Qy    1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy    1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1619
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                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1620

Qy         1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1679
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1680

Qy         1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy         1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy         1800 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1801 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy         1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy         1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy         1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy         2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy         2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy         2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy         2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy         2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy         2340 MEVLGCEAQDLY 2351
                ||||||||||||
Db         2341 MEVLGCEAQDLY 2352.


RESULT 45
AAW11406
ID   AAW11406 standard; Protein; 2352 AA.
XX
AC   AAW11406;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 776 P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Misc-difference 795
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          761..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11444.
XX
PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 25; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy            1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db            1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy           61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db           61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy          121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
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Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGWGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGWGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQPLLFCHISSQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQPLLFCHISSQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGKKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGKKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQPNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQPNATTI 780

Qy        781 PENDIEKTDPWFAH-RTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 839
              ||||||||||||| |||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHPRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 840

Qy        840 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 899
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 900

Qy        900 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 959
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 960

Qy        960 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1019
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1020

Qy        1020 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNLESDTEFKKVTPLIHDRMLMDKNATALR 1079
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1021 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNLESDTEFKKVTPLIHDRMLMDKNATALR 1080

Qy        1080 LNHMSNKTTSSKNMEVVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1139
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1081 LNHMSNKTTSSKNMEVVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1140

Qy        1140 GGGPSPKQLVSLGPEKSVEGQNFLSEKNEVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1199
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1141 GGGPSPKQLVSLGPEKSVEGQNFLSEKNEVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1200

Qy        1200 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1259
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1201 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1260

Qy        1260 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1319
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1261 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1320

Qy        1320 TSQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1321 TSQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy        1380 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1381 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440

Qy        1440 YRKKDSGVQESSSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1441 YRKKDSGVQESSSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500

Qy        1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy        1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1619
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1620

Qy        1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1679
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1680

Qy        1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy        1740 RAQGSGVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1741 RAQGSGVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy        1800 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1801 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy        1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy        1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy        1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy        2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy        2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy        2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy        2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy        2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy        2340 MEVLGCEAQDLY 2351
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                    ||||||||||||
Db          2341 MEVLGCEAQDLY 2352


RESULT 46
AAW11407
ID   AAW11407 standard; Protein; 2352 AA.
XX
AC   AAW11407;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 777 P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Misc-difference 796
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          761..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE, Hung DT, Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 25; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2352 AA;

  Query Match          99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHR-TPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 839
              ||||||||||||||-TPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 839

Db        781 PENDIEKTDPWFAHRPTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 840

Qy        840 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 899
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 900

Qy        900 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 959
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 960
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Qy        960 ENNDSKLLESGLWNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1019
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 ENNDSKLLESGLWNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1020

Qy       1020 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1079
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1080

Qy       1080 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1139
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1140

Qy       1140 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1199
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1200

Qy       1200 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1259
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1260

Qy       1260 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1319
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1320

Qy       1320 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy       1380 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPITVLTRVLPQDNSSHLPAAS 1439
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPITVLTRVLPQDNSSHLPAAS 1440

Qy       1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500

Qy       1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy       1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQITPKEEWKSQEKSPEKTAFKKKDTILS 1619
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQITPKEEWKSQEKSPEKTAFKKKDTILS 1620

Qy       1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1679
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1680

Qy       1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy       1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy       1800 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy       1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy       1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy       1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy       2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy       2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy       2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy       2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy       2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSPTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSPTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy       2340 MEVLGCEAQDLY 2351
              ||||||||||||
Db       2341 MEVLGCEAQDLY 2352
```

```
RESULT 47
AAW11412
ID   AAW11412 standard; Protein; 2352 AA.
XX
AC   AAW11412;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 775 F/E/P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Modified-site   794
FT                   /label= Phe, Glu, Pro
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          760..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11444.
XX
PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
```

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PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 26; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence  2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy        1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy       61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy      121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy      181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy      241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy      301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy      361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy      421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy      481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy      541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy      601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy      661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy      721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy      781 PENDIEKTDPWFA-HRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 839
            ||||||||||||| |||||||||||||||||||||||||||||||||||||||||||||
Db      781 PENDIEKTDPWFAXHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 840

Qy      840 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 899
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      841 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 900

Qy      900 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 959
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      901 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 960

Qy      960 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1019
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      961 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1020

Qy      1020 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1079
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1021 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1080

Qy      1080 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1139
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1081 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1140

Qy      1140 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1199
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1141 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1200

Qy      1200 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1259
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1201 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1260

Qy      1260 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1319
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1261 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1320

Qy      1320 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1321 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy      1380 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1381 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440

Qy      1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500

Qy      1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANN 1559
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANN 1560

Qy      1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1619
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1620

Qy      1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1679
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1680

Qy      1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db        1681 EIDYODTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy        1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799

Db        1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy        1800 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859

Db        1801 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy        1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFTTIFDETKSWYFTENMERNCR 1919

Db        1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFTTIFDETKSWYFTENMERNCR 1920

Qy        1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979

Db        1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy        1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039

Db        1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy        2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099

Db        2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy        2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159

Db        2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy        2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219

Db        2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy        2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279

Db        2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy        2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339

Db        2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy        2340 MEVLGCEAQDLY 2351

Db        2341 MEVLGCEAQDLY 2352


RESULT 48
AAW11417
ID   AAW11417 standard; Protein; 2352 AA.
XX
AC   AAW11417;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 1310 P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Misc-difference 1329
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          761..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE, Hung DT, Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 27; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence  2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
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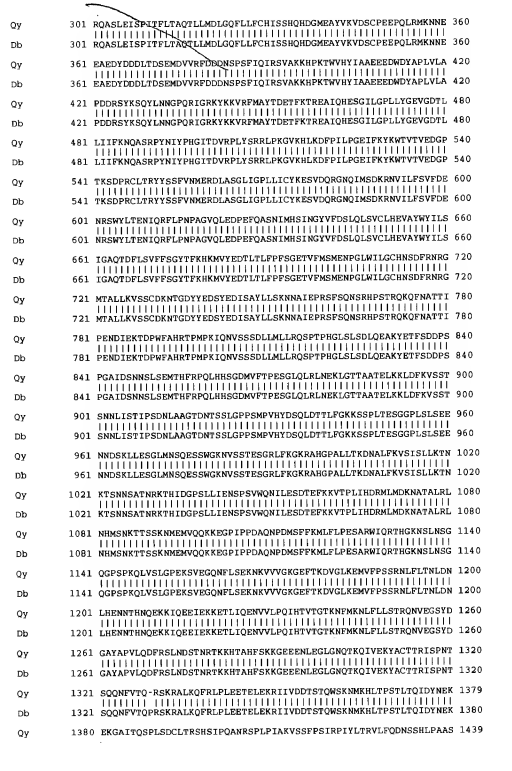

RESULT 49
AAW11418
ID AAW11418 standard; Protein; 2352 AA.
XX
AC AAW11418;

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XX
DT  20-NOV-1997  (first entry)
XX
DE  Active Factor VIII:C analogue residue 1311 P insertion.
XX
KW  Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW  fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW  plasma proteasm; thrombin; immunogen; antibody; haemophiliac; therapy;
KW  proteolytic cleavage.
XX
OS  Homo sapiens.
OS  Synthetic.
XX
FH  Key             Location/Qualifiers
FT  Peptide         1..19
FT                  /note= "signal peptide"
FT  Protein         20..2352
FT                  /note= "mature Factor VIII:C"
FT  Region          20..1668
FT                  /note= "heavy chain fragment"
FT  Misc-difference 1330
FT                  /note= "inserted residue"
FT  Region          1669..2351
FT                  /note= "light chain fragment"
FT  Domain          761..1668
FT                  /note= "B domain"
XX
PN  WO9703195-A1.
XX
PD  30-JAN-1997.
XX
PF  09-JUL-1996;    96WO-US11444.
XX
PR  11-JUL-1995;    95US-0001025.
XX
PA  (CHIR ) CHIRON CORP.
XX
PI  Cohen FE,  Hung DT,  Innis M;
XX
DR  WPI; 1997-119050/11.
XX
PT  Factor VIII:C analog modified adjacent to a non-activating Arg
PT  residue - used in the treatment of haemophiliacs, by improvement of
PT  haemostasis
XX
PS  Claim 27; Page -; 90pp; English.
XX
CC  AAW11330-W11472 represent active Factor VIII:C analogues of the
CC  invention. These sequences were created by mutating the wild type Factor
CC  VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC  analogues comprise a native Factor VIII:C polypeptide modified at a site
CC  adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC  dipeptide is created. Factor VIII:C is a large glycoprotein that
CC  participates in the blood coagulation cascade that ultimately converts
CC  soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC  deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC  X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC  activated by plasma proteases, such as thrombin. During activation the
CC  mature polypeptide is cleaved to generate heavy and light chain fragments
CC  that are further cleaved. Complexes of two or more of the analogues,
CC  nucleic acids and vectors encoding them may be used alone or in
CC  conjunction with each other, for the prevention or treatment of active
CC  Factor VIII:C deficiency in a mammal. The analogues may be used as
CC  immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC  improvement of haemostasis. The analogues are resistant to proteolytic
CC  cleavage and display increased plasma half-life. They may be administered
CC  at lower dosages and by different modes of administration.
XX
SQ  Sequence  2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy    1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
Db    1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy   61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
Db   61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy  121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
Db  121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy  181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
Db  181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy  241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
Db  241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy  301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
Db  301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy  361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
Db  361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy  421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
Db  421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy  481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
Db  481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy  541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
Db  541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy  601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
Db  601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy  661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
Db  661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy  721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
Db  721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy  781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
Db  781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy  841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
Db  841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy  901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
Db  901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy  961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
Db  961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy 1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
Db 1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
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Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSPFKMLPLPESARWIQRTHGKNSLNSG 1140
Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSPFKMLPLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEPTKDVGLKEMVFPSSRNLFLTNLDN 1200
Db       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEPTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLDGLGNQTKQIVEKYACTTRISPNT 1320
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQR-SKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
Db       1321 SQQNFVTQRPSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy       1380 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439
Db       1381 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440

Qy       1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499
Db       1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500

Qy       1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559
Db       1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy       1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKDTILS 1619
Db       1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKDTILS 1620

Qy       1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1679
Db       1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1680

Qy       1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
Db       1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy       1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
Db       1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy       1800 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
Db       1801 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy       1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919
Db       1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy       1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
Db       1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy       1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
Db       1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy       2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
Db       2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy       2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
Db       2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy       2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
Db       2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy       2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
Db       2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy       2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSPTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
Db       2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSPTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy       2340 MEVLGCEAQDLY 2351
Db       2341 MEVLGCEAQDLY 2352


RESULT 50
AAW11389
ID   AAW11389 standard; Protein; 2352 AA.
XX
AC   AAW11389;
XX
DT   18-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 563 P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Misc-difference 582
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          761..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11444.
XX
PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 21; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AA751357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
```

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CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence    2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQR-GNQIMSDKRNVILFSVFD 599
              |||||||||||||||||||||||||||||||||||||||| |||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRPGNQIMSDKRNVILFSVFD 600

Qy        600 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 659
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 660

Qy        660 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 719
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 720

Qy        720 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 779
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 780

Qy        780 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 839
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 840

Qy        840 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 899
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 900

Qy        900 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 959
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 960

Qy        960 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1019
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1020

Qy       1020 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1079
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1080

Qy       1080 LNHMSNKTTSSKNNMEVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1139
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 LNHMSNKTTSSKNNMEVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1140

Qy       1140 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1199
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1200

Qy       1200 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1259
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1260

Qy       1260 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1319
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1320

Qy       1320 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy       1380 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440

Qy       1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500

Qy       1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy       1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1619
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1620

Qy       1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREIRTTLQSDQE 1679
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREIRTTLQSDQE 1680

Qy       1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy       1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy       1800 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860
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Qy       1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy       1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy       1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy       2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy       2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy       2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy       2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy       2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy       2340 MEVLGCEAQDLY 2351
              ||||||||||||
Db       2341 MEVLGCEAQDLY 2352


RESULT 51
AAW11394
ID   AAW11394 standard; Protein; 2352 AA.
XX
AC   AAW11394;
XX
DT   18-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 561 F/E/P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Modified-site   580
FT                   /label= Phe, Glu, Pro
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          761..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11444.
XX
PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE, Hung DT, Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 22; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequences (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence  2352 AA;

  Query Match          99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity  100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy         1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy        61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy       121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy       181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy       241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy       301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       301 RQASLEISPITFLTAQTLLMDDGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy       361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy       421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
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Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVD-QRGNQIMSDKRNVILFSVFD 599

Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDXQRGNQIMSDKRNVILFSVFD 600

Qy        600 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 659

Db        601 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 660

Qy        660 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 719

Db        661 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGIWILGCHNSDFRNR 720

Qy        720 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 779

Db        721 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 780

Qy        780 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 839

Db        781 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 840

Qy        840 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 899

Db        841 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 900

Qy        900 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 959

Db        901 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHTDSQLDTTLFGKKSSPLTESGGPLSLSE 960

Qy        960 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLYKDNALFKVSISLLKT 1019

Db        961 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLYKDNALFKVSISLLKT 1020

Qy       1020 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1079

Db       1021 NKTSNNSANRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1080

Qy       1080 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1139

Db       1081 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1140

Qy       1140 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFTNLD 1199

Db       1141 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFTNLD 1200

Qy       1200 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1259

Db       1201 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1260

Qy       1260 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLNQTKQIVEKYACTTRISPN 1319

Db       1261 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLNQTKQIVEKYACTTRISPN 1320

Qy       1320 TSQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379

Db       1321 TSQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy       1380 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439

Db       1381 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440

Qy       1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499

Db       1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500

Qy       1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559

Db       1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy       1560 PGKVPPLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1619

Db       1561 PGKVPPLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1620

Qy       1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1679

Db       1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1680

Qy       1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739

Db       1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy       1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799

Db       1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy       1800 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859

Db       1801 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy       1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919

Db       1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy       1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979

Db       1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy       1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039

Db       1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy       2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099

Db       2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy       2100 IHGIRTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159

Db       2101 IHGIRTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy       2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219

Db       2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy       2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279

Db       2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy       2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSPTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339

Db       2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSPTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy       2340 MEVLGCEAQDLY 2351

Db       2341 MEVLGCEAQDLY 2352

RESULT 52
AAW11397
ID   AAW11397 standard; Protein; 2352 AA.
XX
AC   AAW11397;
XX
DT   18-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 747 P insertion.
XX
KW   Factor VIII:C analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
```

```
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Misc-difference 766
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          761..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11444.
XX
PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE, Hung DT, Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 23; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AA751357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNS-RHPSTRQKQFNATT 779
              ||||||||||||||||||||||||||||||||||||||||||||| ||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSPRHPSTRQKQFNATT 780

Qy        780 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 839
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 840

Qy        840 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 899
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 900

Qy        900 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 959
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 960

Qy        960 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1019
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1020

Qy        1020 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1079
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db.       1021 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1080

Qy        1080 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1139
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1081 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1140

Qy        1140 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1199
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1141 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1200

Qy        1200 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1259
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1201 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1260
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                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1201 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1260

Qy          1260 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1319
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1261 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1320

Qy          1320 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1321 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy          1380 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1381 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440

Qy          1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500

Qy          1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy          1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1619
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1620

Qy          1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1679
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1680

Qy          1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy          1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy          1800 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1801 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy          1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy          1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy          1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy          2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy          2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy          2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy          2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy          2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy          2340 MEVLGCEAQDLY 2351
                  |||||||||||
Db          2341 MEVLGCEAQDLY 2352
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RESULT 53
AAW11400
ID   AAW11400 standard; Protein; 2352 AA.
XX
AC   AAW11400;
XX
DT   18-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 748 P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Misc-difference 767
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          761..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11444.
XX
PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 23; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
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CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2352 AA;

  Query Match          99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKETQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKETQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHKKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHKKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSR-HPSTRQKQFNATT 779
              ||||||||||||||||||||||||||||||||||||||||||||||| |||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRPHPSTRQKQFNATT 780

Qy        780 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 839
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 840

Qy        840 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 899
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 900

Qy        900 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 959
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 960

Qy        960 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1019
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1020

Qy        1020 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1079
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1021 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1080

Qy        1080 LNHMSNKTTSSKNNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1139
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1081 LNHMSNKTTSSKNNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1140

Qy        1140 GQGPSPKQLVSLGPEKSVEQQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1199
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1141 GQGPSPKQLVSLGPEKSVEQQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1200

Qy        1200 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1259
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1201 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGST 1260

Qy        1260 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLDNQTKQIVEKYACTTRISPN 1319
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1261 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLDNQTKQIVEKYACTTRISPN 1320

Qy        1320 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1321 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy        1380 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1381 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440

Qy        1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500

Qy        1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy        1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1619
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1620

Qy        1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1679
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1680

Qy        1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy        1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy        1800 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1801 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy        1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy        1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy        1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
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                  ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy        2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy        2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy        2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy        2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy        2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy        2340 MEVLGCEAQDLY 2351
               ||||||||||||
Db        2341 MEVLGCEAQDLY 2352
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RESULT 54
AAW11374
ID   AAW11374 standard; Protein; 2352 AA.
XX
AC   AAW11374;
XX
DT   18-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 337 P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key                Location/Qualifiers
FT   Peptide            1..19
FT                      /note= "signal peptide"
FT   Protein            20..2352
FT                      /note= "mature Factor VIII:C"
FT   Region             20..1668
FT                      /note= "heavy chain fragment"
FT   Misc-difference 356
FT                      /note= "inserted residue"
FT   Region             1669..2351
FT                      /note= "light chain fragment"
FT   Domain             761..1668
FT                      /note= "B domain"
FT
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11444.
XX
PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 17; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLR-MKNN 359
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||| ||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRPMKNN 360

Qy        360 EEAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 419
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EEAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 420

Qy        420 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 479
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 480

Qy        480 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 539
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 540

Qy        540 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 599
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 600
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Qy        600 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 659
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 660

Qy        660 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 719
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 720

Qy        720 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 779
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 780

Qy        780 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 839
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 840

Qy        840 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 899
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 900

Qy        900 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 959
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 960

Qy        960 EWNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLVKDNALFKVSISLLKT 1019
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 EWNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLVKDNALFKVSISLLKT 1020

Qy       1020 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKVTPLIHDRMLMDKNATALR 1079
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKVTPLIHDRMLMDKNATALR 1080

Qy       1080 LNHMSNKTTSSKNMEMVQQKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1139
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 LNHMSNKTTSSKNMEMVQQKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1140

Qy       1140 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1199
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1200

Qy       1200 NLHENNTHNQEKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQVNEGSY 1259
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 NLHENNTHNQEKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQVNEGSY 1260

Qy       1260 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1319
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1320

Qy       1320 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy       1380 EKGATQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 EKGATQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440

Qy       1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500

Qy       1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy       1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1619
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1620

Qy       1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1679
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1680

Qy       1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy       1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy       1800 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy       1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCR 1919
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCR 1920

Qy       1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy       1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy       2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy       2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy       2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy       2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy       2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy       2340 MEVLGCEAQDLY 2351
              ||||||||||||
Db       2341 MEVLGCEAQDLY 2352

RESULT 55
AAW11381
ID   AAW11381 standard; Protein; 2352 AA.
XX
AC   AAW11381;
XX
DT   18-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 359 P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
```

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FT                   /note= "heavy chain fragment"
FT   Misc-difference 378
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          761..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 19; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2352 AA;
```

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  Query Match          99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVV-RFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 419
              |||||||||||||||| |||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVPRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 420

Qy        420 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 479
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 480

Qy        480 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 539
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 540

Qy        540 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 599
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 600

Qy        600 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 659
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 660

Qy        660 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 719
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 720

Qy        720 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 779
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 780

Qy        780 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 839
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 840

Qy        840 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 899
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 900

Qy        900 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 959
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 960

Qy        960 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1019
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1020

Qy        1020 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRLMLDKNATALR 1079
               |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1021 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRLMLDKNATALR 1080

Qy        1080 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSPFKMLPLPESARWIQRTHGKNSLNS 1139
               |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1081 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSPFKMLPLPESARWIQRTHGKNSLNS 1140

Qy        1140 GQGPSPKQLVSLGPEKSVEQQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFTNLD 1199
               |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1141 GQGPSPKQLVSLGPEKSVEQQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFTNLD 1200

Qy        1200 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1259
               |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1201 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1260

Qy        1260 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1319
               |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1261 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1320

Qy        1320 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
               |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1321 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380
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Qy       1380 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440

Qy       1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500

Qy       1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy       1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKDTILS 1619
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKDTILS 1620

Qy       1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1679
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1680

Qy       1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy       1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy       1800 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy       1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy       1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy       1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy       2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy       2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy       2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy       2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy       2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy       2340 MEVLGCEAQDLY 2351
                ||||||||||||
Db       2341 MEVLGCEAQDLY 2352


RESULT 56
AAW11382
ID   AAW11382 standard; Protein; 2352 AA.
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XX
AC   AAW11382;
XX
DT   18-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 360 P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Misc-difference 379
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          761..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11444.
XX
PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 19; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AA751357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
```

```
Best Local Similarity  100.0%;  Pred. No. 0;
Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFPLCLLRFCFSATRRYYLGAVELSWDYQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFPLCLLRFCFSATRRYYLGAVELSWDYQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVR-PDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 419
              ||||||||||||||||| |||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRPDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 420

Qy        420 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 479
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 480

Qy        480 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 539
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 540

Qy        540 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 599
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 600

Qy        600 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 659
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 660

Qy        660 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 719
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 720

Qy        720 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 779
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 780

Qy        780 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 839
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 840

Qy        840 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 899
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 900

Qy        900 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 959
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 960

Qy        960 ENNDSKLLSEGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1019
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 ENNDSKLLSEGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1020

Qy       1020 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1079
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

Db       1021 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1080

Qy       1080 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1139
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1140

Qy       1140 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEPTKDVGLKEMVFPSSRNLFTNLD 1199
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEPTKDVGLKEMVFPSSRNLFTNLD 1200

Qy       1200 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1259
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1260

Qy       1260 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1319
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1320

Qy       1320 TSQQNFVTQRSKRALKQFRLPLEETELEKRIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 TSQQNFVTQRSKRALKQFRLPLEETELEKRIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy       1380 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440

Qy       1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500

Qy       1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy       1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKDTILS 1619
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKDTILS 1620

Qy       1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1679
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1680

Qy       1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy       1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy       1800 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAFFSD 1859
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAFFSD 1860

Qy       1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy       1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy       1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy       2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy       2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160
```

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Qy       2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy       2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy       2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy       2340 MEVLGCEAQDLY 2351
                ||||||||||||
Db       2341 MEVLGCEAQDLY 2352


RESULT 57
AAW11385
ID   AAW11385 standard; protein; 2352 AA.
XX
AC   AAW11385;
XX
DT   18-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 358 F/E/P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Modified-site   377
FT                   /label= Phe, Glu, Pro
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          761..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE, Hung DT, Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 20; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. the analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 419
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 420

Qy        420 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 479
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 480

Qy        480 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 539
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 540

Qy        540 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 599
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 600

Qy        600 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 659
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 660

Qy        660 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 719
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 720
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Qy        720 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 779
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 780

Qy        780 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 839
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 840

Qy        840 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 899
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 900

Qy        900 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 959
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 960

Qy        960 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1019
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1020

Qy        1020 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1079
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1021 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1080

Qy        1080 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1139
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1081 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1140

Qy        1140 GQGPSPKQLVSLGPEKSVEQQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1199
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1141 GQGPSPKQLVSLGPEKSVEQQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1200

Qy        1200 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1259
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1201 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1260

Qy        1260 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1319
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1261 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1320

Qy        1320 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1321 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy        1380 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1381 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440

Qy        1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500

Qy        1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy        1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1619
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1620

Qy        1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1679
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1680

Qy        1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy        1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy        1800 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAFSD 1859
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              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1801 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAFSD 1860

Qy        1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy        1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy        1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy        2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy        2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy        2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy        2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy        2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy        2340 MEVLGCEAQDLY 2351
               ||||||||||||
Db        2341 MEVLGCEAQDLY 2352
```

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RESULT 58
AAW11388
ID   AAW11388 standard; Protein; 2352 AA.
XX
AC   AAW11388;
XX
DT   18-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 562 P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Misc-difference 581
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          761..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
```

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XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 21; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence  2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAVVKVDSCPEEPQLRMKNNE 360
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAVVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQ-RGNQIMSDKRNVILFSVFD 599
              |||||||||||||||||||||||||||||||||||||||| |||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 600

Qy        600 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 659
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 660

Qy        660 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 719
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 720

Qy        720 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 779
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 780

Qy        780 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 839
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 840

Qy        840 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 899
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 900

Qy        900 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 959
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 960

Qy        960 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1019
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1020

Qy       1020 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1079
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1080

Qy       1080 LNHMSNKTTSSKNMEMVQQKKEQPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1139
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 LNHMSNKTTSSKNMEMVQQKKEQPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1140

Qy       1140 GQGPSPKQLVSLGPEKSVEQQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1199
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 GQGPSPKQLVSLGPEKSVEQQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1200

Qy       1200 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1259
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1260

Qy       1260 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1319
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1320

Qy       1320 TSQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 TSQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy       1380 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440

Qy       1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500
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```
Qy       1500 PKDDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559
             |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy       1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1619
             |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1620

Qy       1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1679
             |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1680

Qy       1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
             |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy       1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
             |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy       1800 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
             |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy       1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFTTIFDETKSWYFTENMERNCR 1919
             |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFTTIFDETKSWYFTENMERNCR 1920

Qy       1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
             |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy       1980 HVPTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
             |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 HVPTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy       2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
             |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy       2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
             |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy       2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
             |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy       2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
             |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy       2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
             |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy       2340 MEVLGCEAQDLY 2351
             ||||||||||||
Db       2341 MEVLGCEAQDLY 2352


RESULT 59
AAW11357
ID   AAW11357 standard; Protein; 2352 AA.
XX
AC   AAW11357;
XX
DT   17-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 278 F/E/P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Modified-site   297
FT                   /label= Phe, Glu, Pro
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          761..1668
FT                   /note= "B domain"
FT
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 14; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
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Db 61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
Qy 121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
Db 121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
Qy 181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
Db 181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
Qy 241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFL-VRN 299
Db 241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLXVRN 300
Qy 300 HRQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNN 359
Db 301 HRQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNN 360
Qy 360 EEADDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 419
Db 361 EEADDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 420
Qy 420 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 479
Db 421 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 480
Qy 480 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 539
Db 481 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 540
Qy 540 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 599
Db 541 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 600
Qy 600 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 659
Db 601 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 660
Qy 660 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 719
Db 661 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 720
Qy 720 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 779
Db 721 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 780
Qy 780 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 839
Db 781 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 840
Qy 840 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 899
Db 841 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 900
Qy 900 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 959
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Qy 960 ENNDSKLLESGLWNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1019
Db 961 ENNDSKLLESGLWNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1020
Qy 1020 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1079
Db 1021 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1080
Qy 1080 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1139
Db 1081 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1140
Qy 1140 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1199
Db 1141 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1200
Qy 1200 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1259
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Qy 1260 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1319
Db 1261 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1320
Qy 1320 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
Db 1321 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380
Qy 1380 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439
Db 1381 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440
Qy 1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499
Db 1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500
Qy 1500 PKPDLPFTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559
Db 1501 PKPDLPFTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560
Qy 1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1619
Db 1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1620
Qy 1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1679
Db 1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1680
Qy 1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
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Qy 1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
Db 1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800
Qy 1800 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAFFSD 1859
Db 1801 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAFFSD 1860
Qy 1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCR 1919
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Qy 1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
Db 1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980
Qy 1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
Db 1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040
Qy 2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
Db 2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100
Qy 2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
Db 2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160
Qy 2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
Db 2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220
Qy 2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
Db 2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

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Qy       2280 LISSSQDGHGWTLFPQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 LISSSQDGHGWTLFPQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy       2340 MEVLGCEAQDLY 2351
             ||||||||||||
Db       2341 MEVLGCEAQDLY 2352


RESULT 60
AAW11363
ID   AAW11363 standard; Protein; 2352 AA.
XX
AC   AAW11363;
XX
DT   18-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 282 P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Misc-difference 301
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          761..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 15; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy         1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy        61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy       121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
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Db       121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy       181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
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Db       181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy       241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy       301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNN 359
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Db       301 PRQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNN 360

Qy       360 EEAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 419
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Db       361 EEAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 420

Qy       420 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 479
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       421 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 480

Qy       480 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 539
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Db       481 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 540

Qy       540 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 599
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       541 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 600

Qy       600 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 659
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       601 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 660

Qy       660 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 719
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       661 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 720

Qy       720 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 779
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Db       721 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 780

Qy       780 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 839
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Db       781 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 840

Qy       840 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 899
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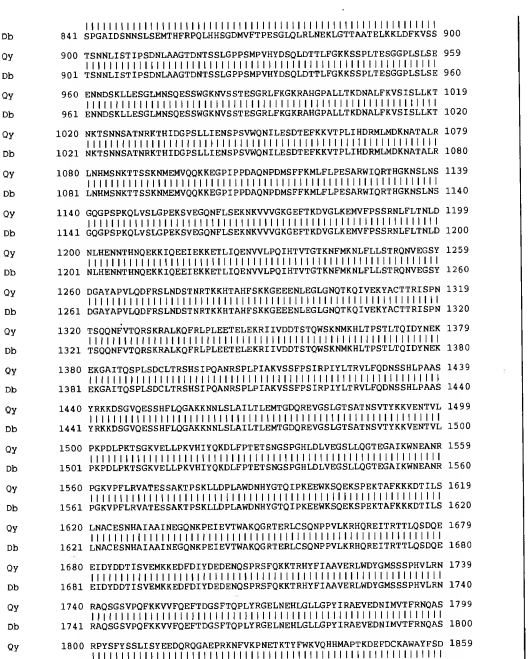

RESULT 61
AAW11364
ID AAW11364 standard; Protein; 2352 AA.
XX
AC AAW11364;
XX
DT 18-NOV-1997 (first entry)
XX
DE Active Factor VIII:C analogue residue 283 P insertion.
XX
KW Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW proteolytic cleavage.
XX
OS Homo sapiens.
OS Synthetic.
XX

FH	Key	Location/Qualifiers
FT	Peptide	1..19
FT		/note= "signal peptide"
FT	Protein	20..2352
FT		/note= "mature Factor VIII:C"
FT	Region	20..1668
FT		/note= "heavy chain fragment"
FT	Misc-difference	302
FT		/note= "inserted residue"
FT	Region	1669..2351
FT		/note= "light chain fragment"
FT	Domain	761..1668
FT		/note= "B domain"

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PN WO9703195-A1.
XX
PD 30-JAN-1997.
XX
PF 09-JUL-1996; 96WO-US11444.
XX
PR 11-JUL-1995; 95US-0001025.
XX
PA (CHIR) CHIRON CORP.
XX

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PI  Cohen FE,  Hung DT,  Innis M;
XX
DR  WPI; 1997-119050/11.
XX
PT  Factor VIII:C analog modified adjacent to a non-activating Arg
PT  residue - used in the treatment of haemophiliacs, by improvement of
PT  haemostasis
XX
PS  Claim 15; Page -; 90pp; English.
XX
CC  AAW11330-W11472 represent active Factor VIII:C analogues of the
CC  invention. These sequences were created by mutating the wild type Factor
CC  VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC  analogues comprise a native Factor VIII:C polypeptide modified at a site
CC  adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC  dipeptide is created. Factor VIII:C is a large glycoprotein that
CC  participates in the blood coagulation cascade that ultimately converts
CC  soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC  deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC  X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC  activated by plasma proteases, such as thrombin. During activation the
CC  mature polypeptide is cleaved to generate heavy and light chain fragments
CC  that are further cleaved. Complexes of two or more of the analogues,
CC  nucleic acids and vectors encoding them may be used alone or in
CC  conjunction with each other, for the prevention or treatment of active
CC  Factor VIII:C deficiency in a mammal. The analogues may be used as
CC  immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC  improvement of haemostasis. The analogues are resistant to proteolytic
CC  cleavage and display increased plasma half-life. They may be administered
CC  at lower dosages and by different modes of administration.
XX
SQ  Sequence  2352 AA;

 Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
 Best Local Similarity   100.0%;  Pred. No. 0;
 Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
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Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 R-QASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNN 359
              | |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RPQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNN 360

Qy        360 EEAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 419
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EEAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 420

Qy        420 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 479
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 480

Qy        480 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 539
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Db        481 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 540

Qy        540 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 599
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 600

Qy        600 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 659
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 660

Qy        660 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 719
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 720

Qy        720 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 779
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 780

Qy        780 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTHPGLSLSDLQEAKYETFSDDP 839
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTHPGLSLSDLQEAKYETFSDDP 840

Qy        840 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 899
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 900

Qy        900 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 959
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Db        901 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 960

Qy        960 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1019
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1020

Qy       1020 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNAIALR 1079
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNAIALR 1080

Qy       1080 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1139
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1140

Qy       1140 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1199
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1200

Qy       1200 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1259
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1260

Qy       1260 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1319
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1320

Qy       1320 TSQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 TSQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy       1380 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440

Qy       1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500

Qy       1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy       1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKDTILS 1619
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKDTILS 1620

Qy       1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1679
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                    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1621 LNACESNHAIAAINEQGNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1680

Qy        1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
                    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy        1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
                    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy        1800 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTFWKVQHHMAPTKDEFDCKAWAYFSD 1859
                    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1801 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy        1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCR 1919
                    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCR 1920

Qy        1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
                    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy        1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
                    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy        2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
                    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy        2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
                    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy        2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
                    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy        2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
                    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy        2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
                    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy        2340 MEVLGCEAQDLY 2351
                    ||||||||||||
Db        2341 MEVLGCEAQDLY 2352


RESULT 62
AAW11368
ID    AAW11368 standard; Protein; 2352 AA.
XX
AC    AAW11368;
XX
DT    18-NOV-1997  (first entry)
XX
DE    Active Factor VIII:C analogue residue 281 F/E/P insertion.
XX
KW    Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW    fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW    plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW    proteolytic cleavage.
XX
OS    Homo sapiens.
OS    Synthetic.
XX
PH    Key             Location/Qualifiers
FT    Peptide         1..19
FT                    /note= "signal peptide"

FT    Protein         20..2352
FT                    /note= "mature Factor VIII:C"
FT    Region          20..1668
FT                    /note= "heavy chain fragment"
FT    Modified-site   300
FT                    /label= Phe, Glu, Pro
FT                    /note= "inserted residue"
FT    Region          1669..2351
FT                    /note= "light chain fragment"
FT    Domain          761..1668
FT                    /note= "B domain"
XX
PN    WO9703195-A1.
XX
PD    30-JAN-1997.
XX
PF    09-JUL-1996;    96WO-US11444.
XX
PR    11-JUL-1995;    95US-0001025.
XX
PA    (CHIR ) CHIRON CORP.
XX
PI    Cohen FE,  Hung DT,  Innis M;
XX
DR    WPI; 1997-119050/11.
XX
PT    Factor VIII:C analog modified adjacent to a non-activating Arg
PT    residue - used in the treatment of haemophiliacs, by improvement of
PT    haemostasis
XX
PS    Claim 16; Page -; 90pp; English.
XX
CC    AAW11330-W11472 represent active Factor VIII:C analogues of the
CC    invention. These sequences were created by mutating the wild type Factor
CC    VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC    analogues comprise a native Factor VIII:C polypeptide modified at a site
CC    adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC    dipeptide is created. Factor VIII:C is a large glycoprotein that
CC    participates in the blood coagulation cascade that ultimately converts
CC    soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC    deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC    X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC    activated by plasma proteases, such as thrombin. During activation the
CC    mature polypeptide is cleaved to generate heavy and light chain fragments
CC    that are further cleaved. Complexes of two or more of the analogues,
CC    nucleic acids and vectors encoding them may be used alone or in
CC    conjunction with each other, for the prevention or treatment of active
CC    Factor VIII:C deficiency in a mammal. The analogues may be used as
CC    immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC    improvement of haemostasis. The analogues are resistant to proteolytic
CC    cleavage and display increased plasma half-life. They may be administered
CC    at lower dosages and by different modes of administration.
XX
SQ    Sequence   2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRN- 299
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||| |
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNX 300

Qy        300 HRQASLEISPTTFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNN 359
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 HRQASLEISPTTFLTAQTLLMDLGQFLLFCHISSHQHDGMEATVKVDSCPEEPQLRMKNN 360

Qy        360 EPAEDTDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEDWDYAPLVL 419
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EPAEDTDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEDWDYAPLVL 420

Qy        420 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 479
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 480

Qy        480 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 539
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 540

Qy        540 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 599
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 600

Qy        600 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 659
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 660

Qy        660 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 719
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 720

Qy        720 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTKQKQFNATT 779
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTKQKQFNATT 780

Qy        780 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 839
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 840

Qy        840 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 899
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 900

Qy        900 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 959
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 960

Qy        960 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1019
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1020

Qy        1020 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1079
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1021 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1080

Qy        1080 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1139
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1081 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1140

Qy        1140 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFTNLD 1199
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1141 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFTNLD 1200

Qy        1200 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1259
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1201 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1260

Qy        1260 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1319
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1261 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1320
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Qy        1320 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1321 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy        1380 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1381 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440

Qy        1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVYTKKVENTVL 1499
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVYTKKVENTVL 1500

Qy        1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy        1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKDTILS 1619
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKDTILS 1620

Qy        1620 LNACESNHAIAAINEQQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITTFTLQSDQE 1679
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1621 LNACESNHAIAAINEQQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITTFTLQSDQE 1680

Qy        1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy        1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy        1800 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1801 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy        1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCR 1919
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCR 1920

Qy        1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy        1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy        2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy        2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy        2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy        2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy        2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy        2340 MEVLGCEAQDLY 2351
               ||||||||||||
Db        2341 MEVLGCEAQDLY 2352
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RESULT 63
AAW11372
ID   AAW11372 standard; Protein; 2352 AA.
XX
AC   AAW11372;
XX
DT   18-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 336 P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Misc-difference 355
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          761..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 17; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0.;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
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Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQL-RMKNN 359
              ||||||||||||||||||||||||||||||||||||||||||||||||||||| ||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLPRMKNN 360

Qy        360 EEAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 419
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Db        361 EEAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 420

Qy        420 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 479
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Db        421 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 480

Qy        480 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 539
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 540

Qy        540 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 599
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 600

Qy        600 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 659
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Db        601 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 660

Qy        660 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 719
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Db        661 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 720

Qy        720 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 779
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Db        721 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 780

Qy        780 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 839
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Db        781 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 840

Qy        840 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 899
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 900

Qy        900 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 959
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Db        901 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 960

Qy        960 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1019
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Db        961 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRANGPALLTKDNALFKVSISLLKT 1020

Qy       1020 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1079

Db       1021 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1080

Qy       1080 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1139

Db       1081 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1140

Qy       1140 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1199

Db       1141 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1200

Qy       1200 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1259

Db       1201 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1260

Qy       1260 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1319

Db       1261 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1320

Qy       1320 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379

Db       1321 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy       1380 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439

Db       1381 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440

Qy       1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499

Db       1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500

Qy       1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559

Db       1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy       1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1619

Db       1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1620

Qy       1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1679

Db       1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1680

Qy       1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739

Db       1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy       1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799

Db       1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy       1800 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859

Db       1801 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy       1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919

Db       1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy       1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979

Db       1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy       1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039

Db       1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy       2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099

Db       2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy       2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159

Db       2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy       2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219

Db       2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy       2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279

Db       2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy       2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339

Db       2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy       2340 MEVLGCEAQDLY 2351

Db       2341 MEVLGCEAQDLY 2352

RESULT 64
AAW11342
ID   AAW11342 standard; Protein; 2352 AA.
XX
AC   AAW11342;
XX
DT   17-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 224 F/E/P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Modified-site   244
FT                   /label= Phe, Glu, Pro
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          761..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
```

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PS   Claim 10; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2352 AA;

  Query Match          99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRNYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRNYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRN 299
              ||| |||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASXARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRN 300

Qy        300 NRQASLETSPTTPLTAQTLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNN 359
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 HRQASLEISPITFLTAQTLMDLGQFLLFCHSSSHQHDGMEAYVKVDSCPEEPQLRMKNN 360

Qy        360 EEAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 419
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EEAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 420

Qy        420 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 479
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Db        421 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 480

Qy        480 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 539
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 540

Qy        540 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 599
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 600

Qy        600 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 659
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Db        601 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 660

Qy        660 SIGAQTDFLSVFPSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 719
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 SIGAQTDFLSVFPSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 720

Qy        720 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 779
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Db        721 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 780

Qy        780 IPENDIEKTDPWPAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 839
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Db        781 IPENDIEKTDPWPAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 840

Qy        840 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 899
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 900

Qy        900 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 959
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 960

Qy        960 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1019
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1020

Qy       1020 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKVVTPLIHDRMLMDKNATALR 1079
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKVVTPLIHDRMLMDKNATALR 1080

Qy       1080 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1139
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1140

Qy       1140 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEPTKDVGLKEMVFPSSRNLFLTNLD 1199
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEPTKDVGLKEMVFPSSRNLFLTNLD 1200

Qy       1200 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1259
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1260

Qy       1260 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1319
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1320

Qy       1320 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy       1380 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440

Qy       1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500

Qy       1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy       1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1619
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1620

Qy       1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1679
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1680

Qy       1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSPHVLRN 1739
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSPHVLRN 1740

Qy       1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
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                    |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy        1800 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
                    |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1801 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy        1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALLFTIFDETKSWYFTENMERNCR 1919
                    |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALLFTIFDETKSWYFTENMERNCR 1920

Qy        1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
                    |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy        1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
                    |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy        2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
                    |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy        2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
                    |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy        2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
                    |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy        2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
                    |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy        2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
                    |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy        2340 MEVLGCEAQDLY 2351
                    ||||||||||||
Db        2341 MEVLGCEAQDLY 2352


RESULT 65
AAW11344
ID   AAW11344 standard; Protein; 2352 AA.
XX
AC   AAW11344;
XX
DT   17-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 249 P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Misc-difference 269
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          761..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11444.
XX
PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 11; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence  2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCH-RKSVYWHVIGMGTTPEVHSIFLEGHTFLVRN 299
              |||||||||||||||||||||||||||| |||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHPRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRN 300

Qy        300 HRQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNN 359
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 HRQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNN 360
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Qy        360 ESAEDVDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 419
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 ESAEDVDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 420

Qy        420 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 479
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 480

Qy        480 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 539
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 540

Qy        540 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 599
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 600

Qy        600 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 659
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 660

Qy        660 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 719
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 720

Qy        720 GMTALLKVSSCDKNTGDYYEDSIYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 779
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 GMTALLKVSSCDKNTGDYYEDSIYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 780

Qy        780 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 839
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 840

Qy        840 SPGAIDSNNSLSEWTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 899
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 SPGAIDSNNSLSEWTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 900

Qy        900 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 959
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 960

Qy        960 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1019
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1020

Qy        1020 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1079
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1021 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1080

Qy        1080 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1139
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1081 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1140

Qy        1140 GGQPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1199
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1141 GGQPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1200

Qy        1200 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1259
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1201 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1260

Qy        1260 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1319
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1261 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1320

Qy        1320 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1321 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy        1380 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1381 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440

Qy        1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500

Qy        1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy        1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1619
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1620

Qy        1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1679
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1680

Qy        1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy        1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy        1800 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1801 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy        1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy        1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy        1980 HVPTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy        2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy        2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy        2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy        2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy        2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy        2340 MEVLGCEAQDLY 2351
               ||||||||||||
Db        2341 MEVLGCEAQDLY 2352


RESULT 66
AAW11345
ID   AAW11345 standard; Protein; 2352 AA.
XX
AC   AAW11345;
XX
DT   17-NOV-1997  (first entry)
XX
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DE   Active Factor VIII:C analogue residue 250 P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Misc-difference 270
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          761..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE, Hung DT, Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 11; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AA75357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding disorder. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence  2352 AA;

  Query Match          99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity  100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHR-KSVYWHVIGMGTTPEVHSIFLEGHTFLVRN 299
              |||||||||||||||||||||||||||| |||||||||||||||||||||||||||||||

Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRPKSVYWHVIGMGTTPEVHSIFLEGHTFLVRN 300

Qy        300 HRQASLSLSPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNN 359
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

Db        301 HRQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNN 360

Qy        360 EEAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 419
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

Db        361 EEAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAEEEDWDYAPLVL 420

Qy        420 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 479
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

Db        421 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 480

Qy        480 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 539
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

Db        481 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 540

Qy        540 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 599
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

Db        541 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 600

Qy        600 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 659
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

Db        601 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 660

Qy        660 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 719
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

Db        661 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 720

Qy        720 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 779
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

Db        721 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 780

Qy        780 IPENDIEKTDPWFARTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 839
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

Db        781 IPENDIEKTDPWFARTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 840

Qy        840 SPGAIDSNNSLSEWTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 899
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

Db        841 SPGAIDSNNSLSEWTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 900

Qy        900 TSNNLISTIPSDNLAAGTDNTSSLGPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 959
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

Db        901 TSNNLISTIPSDNLAAGTDNTSSLGPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 960

Qy        960 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1019
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

Db        961 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1020

Qy       1020 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1079
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

Db       1021 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1080

Qy       1080 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1139
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

Db       1081 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1140
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Qy       1140 GQGPSPKQLVSLGPEKSVEQGNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1199
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 GQGPSPKQLVSLGPEKSVEQGNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1200

Qy       1200 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1259
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1260

Qy       1260 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1319
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1320

Qy       1320 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy       1380 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440

Qy       1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500

Qy       1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy       1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1619
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1620

Qy       1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1679
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1680

Qy       1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy       1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy       1800 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy       1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy       1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy       1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy       2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy       2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy       2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy       2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy       2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy       2340 MEVLGCEAQDLY 2351
             ||||||||||||
Db       2341 MEVLGCEAQDLY 2352
```

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RESULT 67
AAW11350
ID   AAW11350 standard; Protein; 2352 AA.
XX
AC   AAW11350;
XX
DT   17-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 249 F/E/P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Modified-site   268
FT                   /label= Phe, Glu, Pro
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          761..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 12; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
```

CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC activated by plasma proteases, such as thrombin. During activation the
CC mature polypeptide is cleaved to generate heavy and light chain fragments
CC that are further cleaved. Complexes of two or more of the analogues,
CC nucleic acids and vectors encoding them may be used alone or in
CC conjunction with each other, for the prevention or treatment of active
CC Factor VIII:C deficiency in a mammal. The analogues may be used as
CC immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC improvement of haemostasis. The analogues are resistant to proteolytic
CC cleavage and display increased plasma half-life. They may be administered
CC at lower dosages and by different modes of administration.
XX
SQ Sequence 2352 AA;

Query Match 99.9%; Score 12407.5; DB 18; Length 2352;
Best Local Similarity 100.0%; Pred. No. 0;
Matches 2351; Conservative 0; Mismatches 0; Indels 1; Gaps 1;

```
Qy       1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy      61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy     121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy     181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy     241 AASARAWPKMHTVNGYVNRSLPGLIGC-HRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRN 299
           |||||||||||||||||||||||||||| |||||||||||||||||||||||||||||||
Db     241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRN 300

Qy     300 HRQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNN 359
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     301 HRQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNN 360

Qy     360 EEAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 419
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     361 EEAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 420

Qy     420 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 479
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     421 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 480

Qy     480 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 539
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     481 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 540

Qy     540 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 599
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     541 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 600

Qy     600 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 659
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     601 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 660

Qy     660 STGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 719
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     661 STGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 720

Qy     720 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 779
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Db     721 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 780

Qy     780 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLRQSPTPHGLSLSDLQEAKYETFSDDP 839
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     781 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLRQSPTPHGLSLSDLQEAKYETFSDDP 840

Qy     840 SPGAIDSNNSLSEMTHFRPQLHHSGDWVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 899
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     841 SPGAIDSNNSLSEMTHFRPQLHHSGDWVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 900

Qy     900 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 959
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     901 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 960

Qy     960 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1019
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     961 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1020

Qy    1020 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1079
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1021 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1080

Qy    1080 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1139
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1081 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1140

Qy    1140 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1199
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1141 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1200

Qy    1200 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1259
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1201 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1260

Qy    1260 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1319
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1261 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1320

Qy    1320 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1321 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy    1380 EKGAITQSPLSDCLTRSHSIPQAANRSPLPIAKVSSFPSIRPIYLTRVLPQDNSSHLPAAS 1439
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1381 EKGAITQSPLSDCLTRSHSIPQAANRSPLPIAKVSSFPSIRPIYLTRVLPQDNSSHLPAAS 1440

Qy    1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500

Qy    1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy    1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKDTILS 1619
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKDTILS 1620

Qy    1620 LNACESNHAIAAINEQQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1679
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1621 LNACESNHAIAAINEQQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1680

Qy    1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy    1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy    1800 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1801 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy    1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919
           |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db       1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy       1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979

Db       1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy       1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039

Db       1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy       2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099

Db       2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy       2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159

Db       2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy       2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219

Db       2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy       2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279

Db       2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy       2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339

Db       2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy       2340 MEVLGCEAQDLY 2351

Db       2341 MEVLGCEAQDLY 2352


RESULT 68
AAW11353
ID   AAW11353 standard; Protein; 2352 AA.
XX
AC   AAW11353;
XX
DT   17-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 279 P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma proteases; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Misc-difference 298
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          761..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11444.
XX
PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 13; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLV-RN 299

Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRRN 300

Qy        300 HRQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNN 359

Db        301 HRQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNN 360

Qy        360 EEAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 419

Db        361 EEAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 420

Qy        420 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 479

Db        421 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 480
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Qy        480 LLIIFKMQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 539
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LLIIFKMQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 540

Qy        540 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 599
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 600

Qy        600 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 659
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 660

Qy        660 SIGAQTDFLSVPFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 719
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 SIGAQTDFLSVPFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 720

Qy        720 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 779
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 780

Qy        780 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 839
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 840

Qy        840 SPGAIDSNNSLSEMTHFRPQLHHSGDWVPTPESGLQLRLNEKLGTTAATELKKLDFKVSS 899
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 SPGAIDSNNSLSEMTHFRPQLHHSGDWVPTPESGLQLRLNEKLGTTAATELKKLDFKVSS 900

Qy        900 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 959
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 960

Qy        960 ENNDSKLLESGLNNSQESSWGKNVSSTESGRLFGKGHAHGPALLTKDNALFKVSISLLKT 1019
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 ENNDSKLLESGLNNSQESSWGKNVSSTESGRLFGKGHAHGPALLTKDNALFKVSISLLKT 1020

Qy        1020 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1079
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1021 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1080

Qy        1080 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1139
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1081 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1140

Qy        1140 GGGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1199
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1141 GGGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1200

Qy        1200 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1259
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1201 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1260

Qy        1260 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1319
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1261 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1320

Qy        1320 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1321 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy        1380 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1381 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440

Qy        1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500

Qy        1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy        1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKDQTILS 1619
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKDQTILS 1620

Qy        1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1679
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1680

Qy        1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy        1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy        1800 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1801 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy        1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy        1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy        1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy        2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy        2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy        2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy        2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy        2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy        2340 MEVLGCEAQDLY 2351
               ||||||||||||
Db        2341 MEVLGCEAQDLY 2352

RESULT 69
AAW11354
ID   AAW11354 standard; Protein; 2352 AA.
XX
AC   AAW11354;
XX
DT   17-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 280 P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
```

```
XX
PH   Key              Location/Qualifiers
FT   Peptide          1..19
FT                    /note= "signal peptide"
FT   Protein          20..2252
FT                    /note= "mature Factor VIII:C"
FT   Region           20..1668
FT                    /note= "heavy chain fragment"
FT   Misc-difference  299
FT                    /note= "inserted residue"
FT   Region           1669..2251
FT                    /note= "light chain fragment"
FT   Domain           761..1668
FT                    /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 13; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insolubie fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRN 299
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRPN 300

Qy        300 HRQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNN 359
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 HRQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNN 360

Qy        360 EEAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 419
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EEAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 420

Qy        420 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 479
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 480

Qy        480 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 539
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 540

Qy        540 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 599
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 600

Qy        600 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 659
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 660

Qy        660 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 719
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 720

Qy        720 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 779
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Db        721 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 780

Qy        780 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 839
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 840

Qy        840 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 899
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 900

Qy        900 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 959
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 960

Qy        960 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1019
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1020

Qy       1020 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1079
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEPKKVTPLIHDRMLMDKNATALR 1080

Qy       1080 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1139
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSPFKMLFLPESARWIQRTHGKNSLNS 1140

Qy       1140 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEPTKDVGLKEMVFPSSRNLFLTNLD 1199
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEPTKDVGLKEMVFPSSRNLFLTNLD 1200

Qy       1200 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1259
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGST 1260
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Qy       1260 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1319
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1320

Qy       1320 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy       1380 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440

Qy       1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500

Qy       1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy       1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1619
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1620

Qy       1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1679
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1680

Qy       1680 EIDYDDTISVEMKKEDPDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 EIDYDDTISVEMKKEDPDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy       1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy       1800 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy       1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy       1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy       1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy       2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy       2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSGIKHNIF 2159
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSGIKHNIF 2160

Qy       2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy       2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy       2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy       2340 MEVLGCEAQDLY 2351
```

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                 ||||||||||||
Db       2341 MEVLGCEAQDLY 2352

RESULT 70
AAW11330
ID   AAW11330 standard; Protein; 2352 AA.
XX
AC   AAW11330;
XX
DT   17-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 218 F/E/P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Modified-site   238
FT                   /label= Phe, Glu, Pro
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          761..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 8; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
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CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy        1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy       61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy      121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy      181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQ-DR 239
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||| ||
Db      181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQXDR 240

Qy      240 DAASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRN 299
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      241 DAASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRN 300

Qy      300 HRQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNN 359
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      301 HRQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNN 360

Qy      360 EEAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 419
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      361 EEAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 420

Qy      420 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 479
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      421 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 480

Qy      480 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 539
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      481 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 540

Qy      540 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 599
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      541 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 600

Qy      600 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 659
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      601 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 660

Qy      660 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 719
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      661 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 720

Qy      720 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 779
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      721 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 780

Qy      780 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 839
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      781 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 840

Qy      840 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 899
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      841 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 900

Qy      900 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 959
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db      901 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 960

Qy      960 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1019
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      961 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1020

Qy      1020 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1079
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1021 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1080

Qy      1080 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFPKMLFLPESARWIQRTHGKNSLNS 1139
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1081 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFPKMLFLPESARWIQRTHGKNSLNS 1140

Qy      1140 GGQPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1199
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1141 GGQPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1200

Qy      1200 NLSENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1259
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1201 NLSENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1260

Qy      1260 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1319
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1261 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1320

Qy      1320 TSQQNFVTQRSKRALKQFRLPLEETELEKRIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1321 TSQQNFVTQRSKRALKQFRLPLEETELEKRIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy      1380 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1381 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440

Qy      1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500

Qy      1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy      1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1619
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1620

Qy      1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1679
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1680

Qy      1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy      1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy      1800 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1801 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy      1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy      1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy      1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040
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Qy       2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy       2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy       2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy       2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy       2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy       2340 MEVLGCEAQDLY 2351
                ||||||||||||
Db       2341 MEVLGCEAQDLV 2352


RESULT 71
AAW11333
ID   AAW11333 standard; Protein; 2352 AA.
XX
AC   AAW11333;
XX
DT   17-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 219 P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Misc-difference 239
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          761..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 7; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy         1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy        61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy       121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy       181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQD-R 239
             |||||||||||||||||||||||||||||||||||||||||||||||||||||||||| | 
Db       181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDPR 240

Qy       240 DAASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRN 299
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       241 DAASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRN 300

Qy       300 HRQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNN 359
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       301 HRQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNN 360

Qy       360 EEAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 419
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       361 EEAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 420

Qy       420 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 479
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       421 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 480

Qy       480 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 539
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       481 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 540

Qy       540 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 599
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       541 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 600

Qy       600 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 659
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                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          601 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 660

Qy          660 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 719
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          661 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 720

Qy          720 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 779
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          721 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 780

Qy          780 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 839
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          781 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 840

Qy          840 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 899
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          841 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 900

Qy          900 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 959
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          901 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 960

Qy          960 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1019
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          961 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1020

Qy         1020 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1079
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1021 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1080

Qy         1080 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1139
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1081 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1140

Qy         1140 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1199
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1141 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1200

Qy         1200 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1259
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1201 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1260

Qy         1260 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1319
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1261 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1320

Qy         1320 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1321 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy         1380 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1381 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440

Qy         1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500

Qy         1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy         1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1619
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1620

Qy         1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1679
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1680

Qy         1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy         1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy         1800 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1801 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy         1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy         1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy         1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy         2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy         2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy         2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy         2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy         2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy         2340 MEVLGCEAQDLY 2351
                ||||||||||||
Db         2341 MEVLGCEAQDLY 2352

RESULT 72
AAW11334
ID   AAW11334 standard; Protein; 2352 AA.
XX
AC   AAW11334;
XX
DT   17-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 220 P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Misc-difference 240
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FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          761..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen PE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 7; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AA751357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSPFFN 60
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSPFFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDR- 239
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||| |
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRP 240

Qy        240 DAASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRN 299
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 DAASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRN 300

Qy        300 HRQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNN 359
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 HRQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNN 360

Qy        360 EEAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 419
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EEAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 420

Qy        420 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 479
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 480

Qy        480 LLIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 539
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LLIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 540

Qy        540 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 599
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 600

Qy        600 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 659
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 660

Qy        660 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 719
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 720

Qy        720 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 779
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Db        721 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 780

Qy        780 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 839
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Db        781 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 840

Qy        840 SPGAIDSNNSLSEWTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 899
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 SPGAIDSNNSLSEWTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 900

Qy        900 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 959
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 960

Qy        960 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1019
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1020

Qy       1020 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1079
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1080

Qy       1080 LNHMSNKTTSSKNMEMVQQKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTMGKNSLNS 1139
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 LNHMSNKTTSSKNMEMVQQKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1140

Qy       1140 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1199
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1200

Qy       1200 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHVTGTKNFMKNLFLLSTRQNVEGSY 1259
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHVTGTKNFMKNLFLLSTRQNVEGSY 1260

Qy       1260 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1319
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1320

Qy       1320 TSQQNFVTQRSKRALKQFRLPLEETALEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
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Db       1321 TSQQNFVTQRSKRALKQFRLPLEETALEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy       1380 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439
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                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440

Qy       1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500

Qy       1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy       1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1619
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Db       1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1620

Qy       1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1679
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQE 1680

Qy       1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db       1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy       1800 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
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Qy       1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy       1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy       1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy       2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy       2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy       2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy       2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy       2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy       2340 MEVLGCEAQDLY 2351
              ||||||||||||
Db       2341 MEVLGCEAQDLY 2352
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RESULT 73
AAW11336
ID   AAW11336 standard; Protein; 2352 AA.
XX
AC   AAW11336;
XX
DT   17-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 225 P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Misc-difference 245
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          761..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11444.
XX
PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 9; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   x-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;
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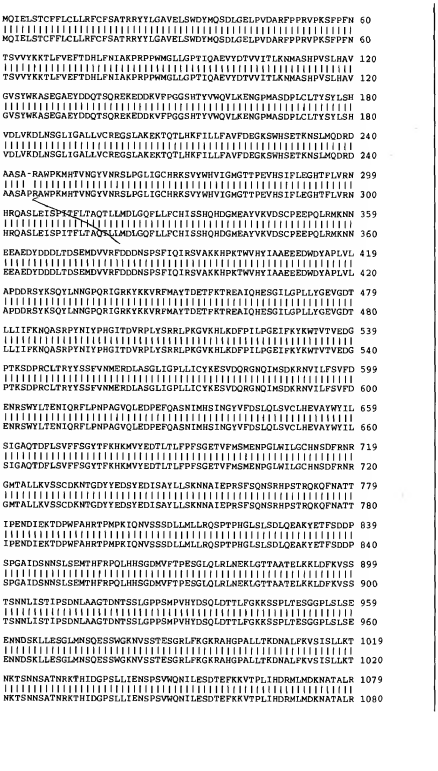
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Db 61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
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Qy 181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
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Qy 300 HRQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNN 359
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Db 361 EEAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 420
Qy 420 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 479
Db 421 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 480
Qy 480 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 539
Db 481 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 540
Qy 540 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 599
Db 541 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 600
Qy 600 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 659
Db 601 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 660
Qy 660 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 719
Db 661 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 720
Qy 720 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 779
Db 721 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 780
Qy 780 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 839
Db 781 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 840
Qy 840 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 899
Db 841 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 900
Qy 900 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 959
Db 901 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 960
Qy 960 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1019
Db 961 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1020
Qy 1020 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1079
Db 1021 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1080
Qy 1080 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1139
Db 1081 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1140
Qy 1140 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1199
Db 1141 GQGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1200
Qy 1200 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1259
Db 1201 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1260
Qy 1260 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1319
Db 1261 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1320
Qy 1320 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
Db 1321 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380
Qy 1380 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439
Db 1381 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440
Qy 1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEWTGDQREVGSLGTSATNSVTYKKVENTVL 1499
Db 1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEWTGDQREVGSLGTSATNSVTYKKVENTVL 1500
Qy 1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559
Db 1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560
Qy 1560 PGKVFPLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1619
Db 1561 PGKVFPLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1620
Qy 1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQRETRTTLQSDQE 1679
Db 1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQRETRTTLQSDQE 1680
Qy 1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
Db 1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740
Qy 1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
Db 1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800
Qy 1800 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
Db 1801 RPYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860
Qy 1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCR 1919
Db 1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCR 1920
Qy 1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
Db 1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980
Qy 1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
Db 1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040
Qy 2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
Db 2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100
Qy 2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
Db 2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160
Qy 2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219

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                    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy        2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy        2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy        2340 MEVLGCEAQDLY 2351
               ||||||||||||
Db        2341 MEVLGCEAQDLY 2352


RESULT 74
AAW11337
ID   AAW11337 standard; Protein; 2352 AA.
XX
AC   AAW11337;
XX
DT   17-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 226 P insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2352
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1668
FT                   /note= "heavy chain fragment"
FT   Misc-difference 246
FT                   /note= "inserted residue"
FT   Region          1669..2351
FT                   /note= "light chain fragment"
FT   Domain          761..1668
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE, Hung DT, Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 9; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2352 AA;

  Query Match             99.9%;  Score 12407.5;  DB 18;  Length 2352;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2351;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARA-AWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRN 299
              ||||| |||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARPAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRN 300

Qy        300 HRQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNN 359
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 HRQASLEISPITFLTAQTLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNN 360

Qy        360 EEAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 419
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EEAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVL 420

Qy        420 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 479
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 APDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDT 480

Qy        480 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 539
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LLIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDG 540

Qy        540 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 599
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 PTKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFD 600

Qy        600 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 659
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 ENRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYIL 660

Qy        660 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 719
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 SIGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNR 720

Qy        720 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 779
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 GMTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATT 780
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Qy        780 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 839
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 IPENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDP 840

Qy        840 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 899
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 SPGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSS 900

Qy        900 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 959
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 TSNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSE 960

Qy        960 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1019
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 ENNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKT 1020

Qy        1020 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1079
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1021 NKTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALR 1080

Qy        1080 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1139
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1081 LNHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNS 1140

Qy        1140 GQGPSPKQLVSLGPEKSVEQQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1199
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1141 GQGPSPKQLVSLGPEKSVEQQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLD 1200

Qy        1200 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1259
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1201 NLHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSY 1260

Qy        1260 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1319
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1261 DGAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPN 1320

Qy        1320 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1379
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1321 TSQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEK 1380

Qy        1380 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1439
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1381 EKGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAAS 1440

Qy        1440 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1499
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1441 YRKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVL 1500

Qy        1500 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1559
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1501 PKPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANR 1560

Qy        1560 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1619
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1561 PGKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILS 1620

Qy        1620 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTLQSDQE 1679
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1621 LNACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTLQSDQE 1680

Qy        1680 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1739
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1681 EIDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRN 1740

Qy        1740 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1799
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1741 RAQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQAS 1800

Qy        1800 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1859
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1801 RPYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSD 1860

Qy        1860 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1919
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1861 VDLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCR 1920

Qy        1920 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1979
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1921 APCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSG 1980

Qy        1980 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2039
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1981 HVFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNK 2040

Qy        2040 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2099
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2041 CQTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMI 2100

Qy        2100 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2159
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2101 IHGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIF 2160

Qy        2160 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2219
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2161 NPPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMF 2220

Qy        2220 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2279
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2221 ATWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEF 2280

Qy        2280 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2339
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2281 LISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALR 2340

Qy        2340 MEVLGCEAQDLY 2351
               ||||||||||||
Db        2341 MEVLGCEAQDLY 2352
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RESULT 75
AAW11352
ID   AAW11352 standard; protein; 2351 AA.
XX
AC   AAW11352;
XX
DT   17-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue C248X.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2351
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Modified-site   267
FT                   /label= Phe, Glu, Pro
FT   Region          1668..2350
FT                   /note= "light chain fragment"
FT   Domain          760..1667
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
```

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PF   09-JUL-1996;   96WO-US11444.
XX
PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE, Hung DT, Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 12; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2351 AA;

  Query Match          99.9%;  Score 12407;  DB 18;  Length 2351;
  Best Local Similarity  100.0%;  Pred. No. 0;
  Matches 2350;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGKHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQVLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQVLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEPTKDVGLKEMVFPSSRNLFLTNLDN 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEPTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSQTQWSKNMKHLTPSTLTQIDYNEKE 1380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSQTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
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Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKRTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKRTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy       1801 PYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 PYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
             |||||||||||
Db       2341 EVLGCEAQDLY 2351
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RESULT 76
AAW11468
ID   AAW11468 standard; protein; 2351 AA.
XX
AC   AAW11468;
XX
DT   21-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue, delta 1720, + residue 1719 insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo saplens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2351
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Region          1668..2350
FT                   /note= "light chain fragment"
FT   Domain          760..1667
FT                   /note= "B domain"
FT   Modified-site   1738
FT                   /label= Phe, Glu, Pro
FT                   /note= "inserted residue"
FT   Misc-difference 1739..1740
FT                   /note= "site of 1 residue deletion"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 38; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2351 AA;

  Query Match             99.9%;  Score 12406;  DB 18;  Length 2351;
  Best Local Similarity   99.9%;  Pred. No. 0;
  Matches 2349;  Conservative    0;  Mismatches    2;  Indels    0;  Gaps    0;

Qy         1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy        61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db        61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy       121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy       181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy       241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy       301 RQASLETSPITFLTAQTLLMDLGQPLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
            |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       301 RQASLEISPITFLTAQTLLMDLGQPLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy       361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy       421 PDDRSYKSQYLNNGPQRIGKKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       421 PDDRSYKSQYLNNGPQRIGKKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy       481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy       541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy       601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy       661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy       721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy       781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy       841 PGAIDSNNSLSEMTHFRPQLHHSGDMVPTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       841 PGAIDSNNSLSEMTHFRPQLHHSGDMVPTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy       901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy       961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLVTKDNALFKVSISLLKTN 1020
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLVTKDNALFKVSISLLKTN 1020

Qy      1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy      1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy      1141 QGPSPKQLVSLGPEKSVEQQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1141 QGPSPKQLVSLGPEKSVEQQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy      1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy      1261 GAYAPVLQDFRSLNDSTNRTKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1261 GAYAPVLQDFRSLNDSTNRTKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy      1321 SQQNEVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1321 SQQNEVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy      1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy      1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy      1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy      1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy      1621 NACESNHAIAAINEQGNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1621 NACESNHAIAAINEQGNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy      1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSPQKRTRHYFIAAVERLWDYGMSSSPHVLRNN 1740
            |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||| |
Db      1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSPQKRTRHYFIAAVERLWDYGMSSSPHVLKRR 1740

Qy      1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy      1801 PYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1801 PYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy      1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCRA 1920
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCRA 1920

Qy      1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy      1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy      2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy      2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy      2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy      2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
```

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Qy       2281 ISSSQDGHQWTLFPQNGKVKVPQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 ISSSQDGHQWTLFPQNGKVKVPQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
                ||||||||||
Db       2341 EVLGCEAQDLY 2351


RESULT 77
AAW11377
ID   AAW11377 standard; Protein; 2351 AA.
XX
AC   AAW11377;
XX
DT   18-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue, delta 335, + residue 334 insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2351
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Modified-site   353
FT                   /label= Phe, Glu, Pro
FT                   /note= "inserted residue"
FT   Misc-difference 354..355
FT                   /note= "site of 1 residue deletion"
FT   Region          1668..2350
FT                   /note= "light chain fragment"
FT   Domain          760..1667
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11444.
XX
PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 18; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AA751357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2351 AA;

  Query Match          .   99.9%;  Score 12406;  DB 18;  Length 2351;
  Best Local Similarity   99.9%;  Pred. No. 0;
  Matches 2349;  Conservative    0;  Mismatches    2;  Indels    0;  Gaps    0;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
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Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKVTPLIHDRMLMDKNATALRL 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
              |||||||||||
Db       2341 EVLGCEAQDLY 2351
```

```
RESULT 78
AAW11376
ID   AAW11376 standard; Protein; 2350 AA.
XX
AC   AAW11376;
XX
DT   18-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue delta 335.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2350
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Modified-site   353..354
FT                   /note= "site of 1 residue deletion"
FT   Region          1668..2349
FT                   /note= "light chain fragment"
FT   Domain          760..1667
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11444.
XX
PR   11-JUL-1995;   95US-0001025.
XX
```

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PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 18; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AA751357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2350 AA;

 Query Match             99.9%;  Score 12403.5;  DB 18;  Length 2350;
 Best Local Similarity   100.0%;  Pred. No. 0.;
 Matches 2350;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQ-RMKNNE 359

Qy        361 EAEDYDDDLTDSEMDVVRFDDQNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        360 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 419

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        420 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 479

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

Db        480 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 539

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        540 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 599

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        600 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 659

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        660 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 719

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        720 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 779

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        780 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 839

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        840 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 899

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        900 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 959

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        960 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1019

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1020 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1079

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1080 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1139

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLPLTNLDN 1200
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1140 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLPLTNLDN 1199

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1200 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1259

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1260 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1319

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1320 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1379

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1380 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1439

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1440 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1499

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1500 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1559

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1560 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1619
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Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1620 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1679

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1680 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1739

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1740 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1799

Qy       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1800 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1859

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCRA 1920
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1860 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCRA 1919

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1920 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1979

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1980 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2039

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPWII 2100
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2040 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPWII 2099

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2100 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2159

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2160 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2219

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2220 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2279

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2280 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2339

Qy       2341 EVLGCEAQDLY 2351
                ||||||||||
Db       2340 EVLGCEAQDLY 2350


RESULT 79
AAW11358
ID   AAW11358 standard; Protein; 2350 AA.
XX
AC   AAW11358;
XX
DT   17-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue delta 277.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers

FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2350
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Modified-site   295..296
FT                   /note= "site of 1 residue deletion"
FT   Region          1668..2349
FT                   /note= "light chain fragment"
FT   Domain          760..1667
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11444.
XX
PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 14; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2350 AA;

  Query Match             99.9%;  Score 12403.5;  DB 18;  Length 2350;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2350;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
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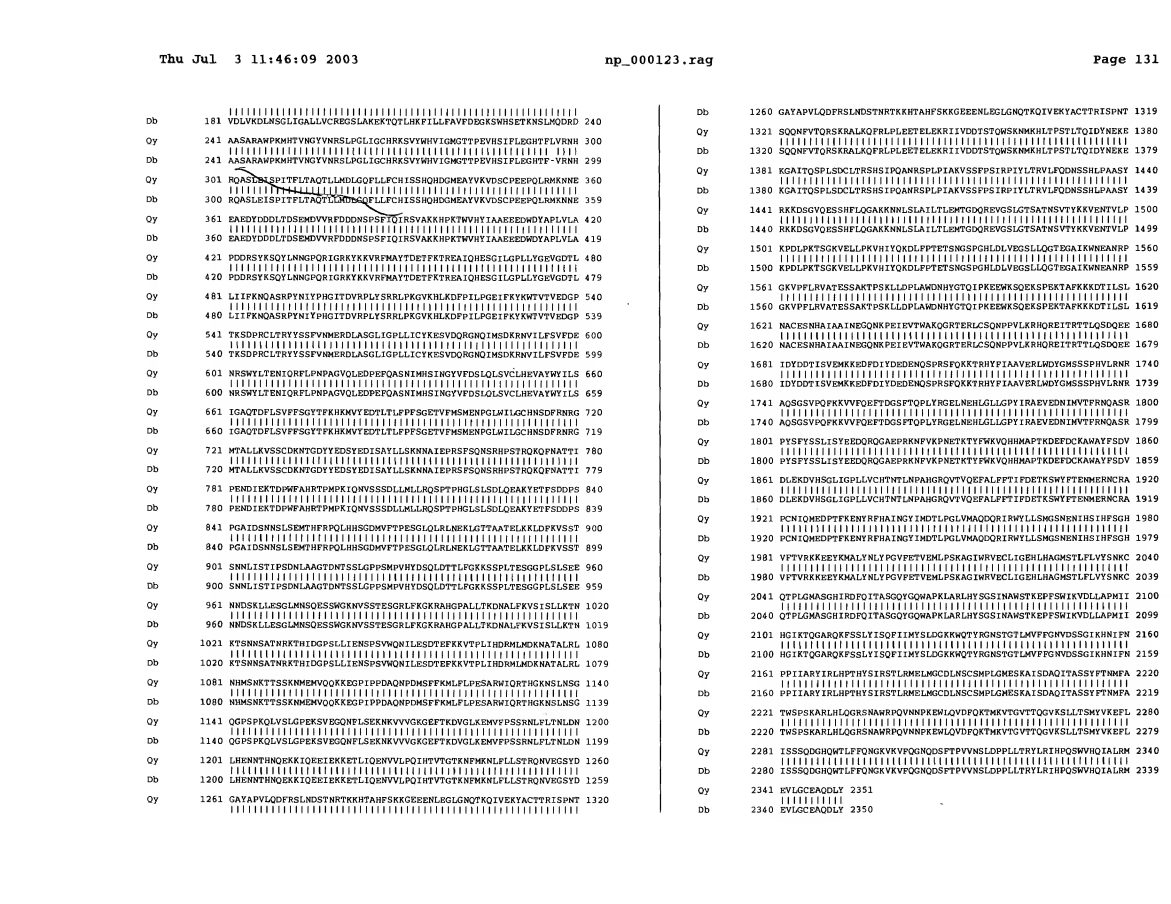

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RESULT 80
AAW11359
ID   AAW11359 standard; Protein; 2350 AA.
XX
AC   AAW11359;
XX
DT   17-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue delta 278.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2350
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Modified-site   296..297
FT                   /note= "site of 1 residue deletion"
FT   Region          1668..2349
FT                   /note= "light chain fragment"
FT   Domain          760..1667
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 14; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence  2350 AA;

  Query Match             99.9%;  Score 12403.5;  DB 18;  Length 2350;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2350;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFL-RNH 299

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        300 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 359

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        360 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 419

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        420 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 479

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        480 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 539

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        540 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 599

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        600 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 659

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        660 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 719

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        720 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 779

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        780 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 839

Qy        841 PGAIDSNNSLSEWTHFRPQLHHSGDWVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        840 PGAIDSNNSLSEWTHFRPQLHHSGDWVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 899

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        900 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 959

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
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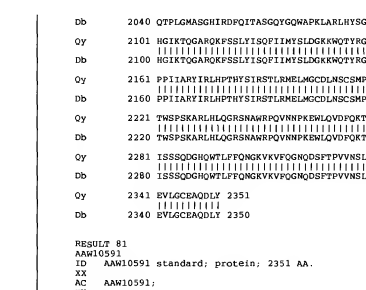

RESULT 81
AAW10591
ID AAW10591 standard; protein; 2351 AA.
XX
AC AAW10591;
XX
DT 03-DEC-1997 (first entry)
XX
DE Factor VIII:C (Phe652His).
XX
KW Factor VIII:C; F8C; Factor V A; Factor V C; domain; F8C deficiency; haemophilia A; blood clotting disorder; immunogen; antibody.
XX
OS Homo sapiens.
XX
FH Key Location/Qualifiers
FT Peptide 1..19
FT /note= "Signal peptide"
FT Protein 20..2351
FT /note= "Mature factor VIII:C"
FT Misc-difference 671
FT /label= Phe652His
XX
PN WO9703191-A1.
XX
PD 30-JAN-1997.
XX
PF 28-JUN-1996; 96WO-US11013.
XX
PR 11-JUL-1995; 95US-0001030.
XX
PA (CHIR) CHIRON CORP.
XX
PI Hung DT;
XX
DR WPI; 1997-119047/11.
XX
PT Factor VIII:C analogue - modified to comprise Factor V A or C domain
PT or subdomain, for increased stability or activity
XX
PS Claim 6; Page -; 45pp; English.
XX
CC The sequences given in W10590-92 represent active Factor VIII:C (F8C)
CC polypeptide analogues. These analogues comprises a native F8C
CC polypeptide modified to comprise the presence of a Factor V A and/or
CC C domain and/or subdomain. The F8C polypeptide analogues, alone or in
CC combination, can be used for the prevention or treatment of an active
CC F8C deficiency, i.e. haemophilia A and other blood clotting disorders.
CC The analogue can also be used as an immunogen for antibody production.
CC The analogues can have an increased plasma half-life, or specific

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CC   activity.  This sequence is not given in the specification and is
CC   based on the sequence derived from Genbank ref. K01740.
XX
SQ   Sequence   2351 AA;

  Query Match             99.9%;  Score 12402;  DB 18;  Length 2351;
  Best Local Similarity   99.9%;  Pred. No. 0;
  Matches 2348;  Conservative    2;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTVHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTVHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||:|||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 IGAQTDFLSVYFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNFDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNFDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVLSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVLSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              :||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||:
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYE 1260

Qy.      1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLDNQTKQIVEKYACTTRISPNT 1320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLDNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGATTQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGATTQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy       1801 PYSFYSSLISYEEDQRGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 PYSFYSSLISYEEDQRGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
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                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy         2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy         2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy         2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy         2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy         2341 EVLGCEAQDLY 2351
                |||||||||||
Db         2341 EVLGCEAQDLY 2351


RESULT 82
AAW13496
ID   AAW13496 standard; Protein; 2351 AA.
XX
AC   AAW13496;
XX
DT   03-DEC-1997  (first entry)
XX
DE   Factor VIII:C (Arg1689Lys).
XX
KW   Factor VIII:C; analogue; substitution; Factor VIII:C deficiency;
KW   mammal; haemophilia A.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 1708
FT                   /label= Arg1689Lys
XX
PN   WO9703194-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11441.
XX
PR   11-JUL-1995;   95US-0001029.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Burke RL,  Rosenberg S;
XX
DR   WPI; 1997-119049/11.
DR   N-PSDB; AAT61548.
XX
PT   Factor VIII:C analogue with Arg 1689 substituted by Lys - useful for
PT   preventing and treating a Factor VIII:C deficiency, particularly
PT   haemophilia A
XX
PS   Claim 1; Page -; 46pp; English.
XX
CC   This sequence represents an active Factor VIII:C polypeptide analogue.
CC   The analogue comprises a native Factor VIII:C polypeptide that is
CC   modified by substitution of the Arg residue at position 1689 with
CC   Lys. The polypeptide analogue can be used to prevent and treat a
CC   Factor VIII:C deficiency in a mammal, esp. haemophilia A.  This
CC   sequence is not given in the specification and is based on the
CC   sequence given in Genbank Ref. K01740.
XX
SQ   Sequence   2351 AA;

  Query Match             99.9%;  Score 12402;  DB 18;  Length 2351;
  Best Local Similarity   99.9%;  Pred. No. 0;
  Matches 2348;  Conservative    2;  Mismatches    1;  Indels    0;  Gaps    0;

Qy            1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db            1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy           61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
                |||||||||||||| |||||||||||||||||||||||||||||||||||||||||||||
Db           61 TSVVYKKTLFVEFTVHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy          121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy          181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy          241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy          301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy          361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy          421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy          481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy          541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy          601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy          661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy          721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy          781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy          841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy          901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy          961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
```

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Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||:
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYE 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKEDTILSL 1620
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKEDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 IDYDDTISVEMKEDFDIYDEDENQSPKSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 VFTVRKKEEYKMALYNLFPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRLRIHPQSWVHQIALRM 2340
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEADDLY 2351
             ||||||||||| 
Db       2341 EVLGCEADDLY 2351
```

RESULT 83
AAY21676
ID AAY21676 standard; Protein; 2351 AA.
XX
AC AAY21676;
XX
DT 18-AUG-1999 (first entry)
XX
DE Factor VIII protein full length sequence.
XX
KW Factor VIII protein; gene modification; gene therapy; clinical disorder;
KW splicing pattern; RNA processing; gene regulation; beta-domain; human.
XX
OS Homo sapiens.
XX
PN WO9929848-A1.
XX
PD 17-JUN-1999.
XX
PF 25-NOV-1998; 98WQ-US25354.
XX
PR 16-JAN-1998; 98US-0071596.
PR 05-DEC-1997; 97US-0067614.
XX
PA (IMMU-) IMMUNE RESPONSE CORP.
XX
PI Bidlingmaier S, Gonzales JEN, Ill CR, Yang CQ;
XX
DR WPI; 1999-385602/32.
DR N-PSDB; AAX82261.
XX
PT Genes and vectors exhibiting increased expression and novel splicing
PT patterns, useful for expression of, e.g. beta-domain deleted factor
PT VIII
XX
PS Example 1; Page 101-115; 123pp; English.
XX
CC The invention describes novel genes and vectors exhibiting increased
CC expression and novel splicing patterns. It provides a gene encoding a
CC Factor VIII protein, that comprises one or more consensus or near
CC consensus splice sites which have been corrected to increase expression.
CC The method, DNA sequences and expression vectors can be used to increase
CC the expression of a gene, especially a Factor VIII gene. Genes containing
CC modified 5' and/or 3' untranslated regions have optimized expression
CC levels and tissue-specific expression. The methods are used for
CC identification and correction of consensus splice sites, addition of
CC introns, optimization of 5' and 3' untranslated regions and increase in
CC cytoplasmic RNA accumulation. Hence the DNAs are useful in gene therapy
CC to treat a clinical disorder, to study RNA processing and/or gene
CC regulation. The present sequence represents the full length factor VIII
CC protein (construct pLZ-6).
XX
SQ Sequence 2351 AA;

```
Query Match              99.9%;  Score 12402;  DB 20;  Length 2351;
Best Local Similarity    99.9%;  Pred. No. 0;
Matches 2348;  Conservative      2;  Mismatches     1;  Indels     0;  Gaps     0;

Qy       1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
           ||:|||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 MEIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy      61 TSVVYKKTLVFEFTDHLFNIAKPRPWWGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 TSVVYKKTLVFEFTDHLFNIAKPRPWWGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy     121 GVSYWKASEGAETDDQTSQRKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 GVSYWKASEGAETDDQTSQRKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy     181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy     241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy     301 RQASLESSPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     301 RQASLESSPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy     361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy     421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy     481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy     541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy     601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy     661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy     721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy     781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy     841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy     901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy     961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy    1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy    1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy    1141 QGPSPKQLVSLGPEKSVEQGNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1141 QGPSPKQLVSLGPEKSVEQGNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy    1201 LHENNTHNQEKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1201 LHENNTHNQEKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy    1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLGGLGNQTKQIVEKYACTTRISPNT 1320
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLGGLGNQTKQIVEKYACTTRISPNT 1320

Qy    1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy    1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy    1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy    1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy    1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy    1621 NACESNHAIAAINEQGNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1621 NACESNHAIAAINEQGNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy    1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy    1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy    1801 PYSFYSSLISYEEDQRGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1801 PYSFYSSLISYEEDQRGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy    1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFTVIFDETKSWYFTENMERNCRA 1920
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFTVIFDETKSWYFTENMERNCRA 1920

Qy    1921 PCNIQMEDPTFKENYFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFGHQ 1980
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1921 PCNIQMEDPTFKENYFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFGHQ 1980

Qy    1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy    2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy    2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
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                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy        2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy        2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy        2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy        2341 EVLGCEAQDLY 2351
               |||||||||||
Db        2341 EVLGCEAQDLY 2351


RESULT 84
AAW10592
ID   AAW10592 standard; protein; 2351 AA.
XX
AC   AAW10592;
XX
DT   03-DEC-1997  (first entry)
XX
DE   Factor VIII:C (Tyr1786His).
XX
KW   Factor VIII:C; F8C; Factor V A; Factor V C; domain; F8C deficiency;
KW   haemophilia A; blood clotting disorder; immunogen; antibody.
XX
OS   Homo sapiens.
XX
FH   Key                Location/Qualifiers
FT   Peptide            1..19
FT                      /note= "Signal peptide"
FT   Protein            20..2351
FT                      /note= "Mature factor VIII:C"
FT   Misc-difference 1805
FT                      /label= Tyr1786His
XX
PN   WO9703191-A1.
XX
PD   30-JAN-1997.
XX
PF   28-JUN-1996;   96WO-US11013.
XX
PR   11-JUL-1995;   95US-0001030.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Hung DT;
XX
DR   WPI; 1997-119047/11.
XX
PT   Factor VIII:C analogue - modified to comprise Factor V A or C domain
PT   or subdomain, for increased stability or activity
XX
PS   Claim 6; Page -; 45pp; English.
XX
CC   The sequences given in W10590-92 represent active Factor VIII:C (F8C)
CC   polypeptide analogues.  These analogues comprises a native F8C
CC   polypeptide modified to comprise the presence of a Factor V A and/or
CC   C domain and/or subdomain.  The F8C polypeptide analogues, alone or in
CC   combination, can be used for the prevention or treatment of an active
CC   F8C deficiency, i.e. haemophilia A and other blood clotting disorders.
CC   The analogue can also be used as an immunogen for antibody production.
CC   The analogues can have an increased plasma half-life, or specific
CC   activity.  This sequence is not given in the specification and is
CC   based on the sequence derived from Genbank ref. K01740.
XX
SQ   Sequence   2351 AA;

  Query Match             99.9%;  Score 12400;  DB 18;  Length 2351;
  Best Local Similarity   99.9%;  Pred. No. 0;
  Matches 2348;  Conservative    2;  Mismatches    1;  Indels    0;  Gaps    0;

Qy           1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db           1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy          61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
               |||||||||||||| |||||||||||||||||||||||||||||||||||||||||||||
Db          61 TSVVYKKTLFVEFTVHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy         121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy         181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy         241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy         301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy         361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy         421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy         481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy         541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy         601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy         661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy         721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy         781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy         841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy         901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy         961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
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Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRLMLDKNATALRL 1080
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRLMLDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGRNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||:
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYE 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
              ||||:|||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 PYSFHSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
              ||||||||||| 
Db       2341 EVLGCEAQDLY 2351


RESULT 85
AAW11471
ID   AAW11471 standard; Protein; 2351 AA.
XX
AC   AAW11471;
XX
DT   21-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue, R336X, R1719X, R1721X.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2350
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Modified-site   355
FT                   /label= Pro, Glu, Asp, Asn, Gln, Ser, Tyr
FT   Domain          759..1667
FT                   /note= "B domain"
FT   Region          1668..2349
FT                   /note= "light chain fragment"
FT   Modified-site   1738
FT                   /label= Pro, Glu, Asp, Asn, Gln, Ser, Tyr
FT   Modified-site   1740
FT                   /label= Glu, Asp, Asn, Gln, Ser, Tyr
XX
PN   WO9703195-A1.
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PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen PE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
```

```
PT   haemostasis
XX
PS   Claim 39; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence  2351 AA;

  Query Match             99.9%;  Score 12400;  DB 18;  Length 2351;
  Best Local Similarity   99.9%;  Pred. No. 0;
  Matches 2348;  Conservative    0;  Mismatches    3;  Indels    0;  Gaps    0;

Qy        1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy       61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy      121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
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Db      121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy      181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
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Db      181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy      241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy      301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy      361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
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Db      361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy      421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
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Db      421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy      481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy      541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
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Db      541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy      601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
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Db      601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy      661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
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Db      661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy      721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
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Db      721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy      781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
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Db      781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy      841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy      901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
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Db      901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy      961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy     1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
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Db     1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy     1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy     1141 QGPSPKQLVSLGPEKSVEQGNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
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Db     1141 QGPSPKQLVSLGPEKSVEQGNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy     1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
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Db     1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy     1261 GAYAPVLQDPRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
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Db     1261 GAYAPVLQDPRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy     1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy     1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy     1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy     1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy     1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
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Db     1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy     1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy     1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
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Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
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Db       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
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Qy       2161 PPIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
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Db       2161 PPIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
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Qy       2341 EVLGCEAQDLY 2351
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Db       2341 EVLGCEAQDLY 2351


RESULT 86
AAW11413
ID   AAW11413 standard; Protein; 2350 AA.
XX
AC   AAW11413;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue delta 774.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2350
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1666
FT                   /note= "heavy chain fragment"
FT   Modified-site   792..793
FT                   /note= "site of 1 residue deletion"
FT   Region          1667..2349
FT                   /note= "light chain fragment"
FT   Domain          760..1666
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE, Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 26; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2350 AA;

  Query Match          99.9%;  Score 12399.5;  DB 18;  Length 2350;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 2350;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
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Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
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Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHKKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHKKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
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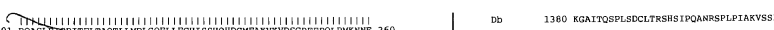

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Db       301 RQASLETSPTFFLTAQTLMDLQQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
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Qy       421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
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Qy       481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
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Qy       541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
Db       541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
Qy       601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
Db       601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
Qy       661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
Db       661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
Qy       721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
Db       721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
Qy       781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
Db       781 PENDIEKTDPWFA-RTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 839
Qy       841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
Db       840 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 899
Qy       901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
Db       900 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 959
Qy       961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
Db       960 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1019
Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
Db       1020 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1079
Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
Db       1080 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1139
Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
Db       1140 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1199
Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
Db       1200 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1259
Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
Db       1260 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1319
Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
Db       1320 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1379
Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
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Db       1380 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1439
Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
Db       1440 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1499
Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
Db       1500 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1559
Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
Db       1560 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1619
Qy       1621 NACESNHAIAAINEQGNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
Db       1620 NACESNHAIAAINEQGNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1679
Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
Db       1680 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1739
Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVFRNQASR 1800
Db       1740 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVFRNQASR 1799
Qy       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
Db       1800 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1859
Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
Db       1860 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1919
Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
Db       1920 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1979
Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
Db       1980 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2039
Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
Db       2040 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2099
Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
Db       2100 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2159
Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
Db       2160 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2219
Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
Db       2220 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2279
Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
Db       2280 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2339
Qy       2341 EVLGCEAQDLY 2351
Db       2340 EVLGCEAQDLY 2350
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RESULT 87
AAW11443
ID AAW11443 standard; Protein; 2349 AA.
XX
AC AAW11443;
XX

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DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 1642, 1643 deletion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2349
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1665
FT                   /note= "heavy chain fragment"
FT   Misc-difference 1660..1661
FT                   /note= "site of 2 residue deletion"
FT   Region          1666..2348
FT                   /note= "light chain fragment"
FT   Domain          760..1665
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 32; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence  2349 AA;

  Query Match             99.8%;  Score 12399;  DB 18;  Length 2349;
  Best Local Similarity   99.9%;  Pred. No. 0;
  Matches 2349;  Conservative    0;  Mismatches    0;  Indels    2;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
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                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy        1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy        1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy        1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy        1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy        1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy        1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy        1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy        1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy        1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
               ||||||||||||||||||||||||||||||||||||||||  ||||||||||||||||||
Db        1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPP--KRHQREITRTTLQSDQEE 1678

Qy        1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1679 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1738

Qy        1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1739 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1798

Qy        1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1799 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1858

Qy        1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1859 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1918

Qy        1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1919 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1978

Qy        1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1979 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2038

Qy        2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2039 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2098

Qy        2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2099 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2158

Qy        2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2159 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2218

Qy        2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2219 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2278

Qy        2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2279 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2338

Qy        2341 EVLGCEAQDLY 2351
               |||||||||||
Db        2339 EVLGCEAQDLY 2349
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RESULT 88
AAW11472
ID   AAW11472 standard; Protein; 2351 AA.
XX
AC   AAW11472;
XX
DT   21-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue, R336P, R1719P, R1721E.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2350
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Modified-site   355
FT                   /label= R336P
FT   Domain          759..1667
FT                   /note= "B domain"
FT   Region          1668..2349
FT                   /note= "light chain fragment"
FT   Modified-site   1738
FT                   /label= R1719P
FT   Modified-site   1740
FT                   /label= R1721E
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11444.
XX
PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 40; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
```

CC VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC analogues comprise a native Factor VIII:C polypeptide modified at a site
CC adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC dipeptide is created. Factor VIII:C is a large glycoprotein that
CC participates in the blood coagulation cascade that ultimately converts
CC soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC activated by plasma proteases, such as thrombin. During activation the
CC mature polypeptide is cleaved to generate heavy and light chain fragments
CC that are further cleaved. Complexes of two or more of the analogues,
CC nucleic acids and vectors encoding them may be used alone or in
CC conjunction with each other, for the prevention or treatment of active
CC Factor VIII:C deficiency in a mammal. The analogues may be used as
CC immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC improvement of haemostasis. The analogues are resistant to proteolytic
CC cleavage and display increased plasma half-life. They may be administered
CC at lower dosages and by different modes of administration.
XX
SQ Sequence 2351 AA;

Query Match 99.8%; Score 12399; DB 18; Length 2351;
Best Local Similarity 99.9%; Pred. No. 0;
Matches 2348; Conservative 0; Mismatches 3; Indels 0; Gaps 0;

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Qy       1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy      61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy     121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy     181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy     241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy     301 RQASLETSPQIFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLPMKNNE 360

Qy     361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy     421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy     481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy     541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy     601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy     661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy     721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTQKQFNATTI 780
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTQKQFNATTI 780

Qy     781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy     841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy     901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy     961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy    1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy    1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy    1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy    1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy    1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLDNQTKQIVEKYACTTRISPNT 1320
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLDNQTKQIVEKYACTTRISPNT 1320

Qy    1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy    1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy    1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy    1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy    1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKDTILSL 1620
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKDTILSL 1620

Qy    1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy    1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLPNE 1740

Qy    1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy    1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
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              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
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Db       2341 EVLGCEAQDLY 2351
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RESULT 89
AAW11424
ID   AAW11424 standard; Protein; 2349 AA.
XX
AC   AAW11424;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 1307, 1308 deletion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2349
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1665
FT                   /note= "heavy chain fragment"
FT   Misc-difference 1326..1327
FT                   /note= "site of 2 residue deletion"
FT   Region          1666..2348
FT                   /note= "light chain fragment"
FT   Domain          760..1665
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11444.
XX
PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 28; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2349 AA;

  Query Match             99.8%;  Score 12398;  DB 18;  Length 2349;
  Best Local Similarity   99.9%;  Pred. No. 0;
  Matches 2349;  Conservative    0;  Mismatches    0;  Indels    2;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
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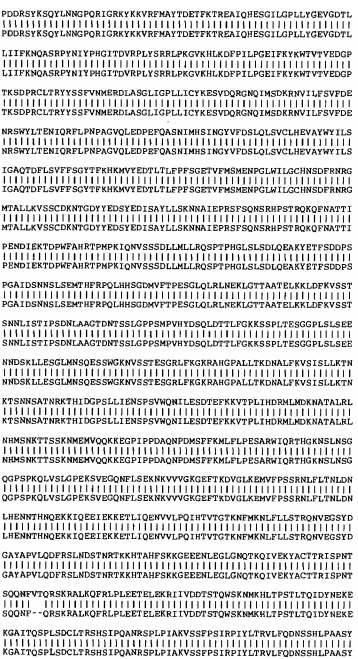

RESULT 90
AAW11373
ID AAW11373 standard; Protein; 2349 AA.
XX
AC AAW11373;
XX
DT 18-NOV-1997 (first entry)
XX
DE Active Factor VIII:C analogue residue 334, 335 deletion.
XX
KW Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;

```
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2349
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1665
FT                   /note= "heavy chain fragment"
FT   Misc-difference 352..353
FT                   /note= "site of 2 residue deletion"
FT   Region          1666..2348
FT                   /note= "light chain fragment"
FT   Domain          758..1665
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 17; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence  2349 AA;

  Query Match             99.8%;  Score 12398;  DB 18;  Length 2349;
  Best Local Similarity   99.9%;  Pred. No. 0;
  Matches 2349;  Conservative    0;  Mismatches    0;  Indels    2;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEP--RMKNNE 358

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        359 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 418

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDEFFTREAIQHESGILGPLLYGEVGDTL 480
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        419 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDEFFTREAIQHESGILGPLLYGEVGDTL 478

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        479 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 538

Qy        541 TKSDPRCLTRYYSSPVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        539 TKSDPRCLTRYYSSPVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 598

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        599 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 658

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        659 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 718

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        719 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 778

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        779 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 838

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        839 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 898

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        899 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 958

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        959 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1018

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1019 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1078

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1079 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1138

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1139 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1198
```

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Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1199 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1258

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1259 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1318

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1319 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1378

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1379 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1438

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1439 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1498

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1499 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1558

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQITPKEEWKSQEKSPEKTAFKKKDTILSL 1620
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1559 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQITPKEEWKSQEKSPEKTAFKKKDTILSL 1618

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1619 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1678

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1679 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1738

Qy       1741 AQSGSVPQFKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1739 AQSGSVPQFKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1798

Qy       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1799 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1858

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1859 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1918

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1919 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1978

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1979 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2038

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2039 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2098

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2099 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2158

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2159 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2218

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2219 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2278

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2279 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2338

Qy       2341 EVLGCEAQDLY 2351
             ||||||||||
Db       2339 EVLGCEAQDLY 2349


RESULT 91
AAW10590
ID   AAW10590 standard; protein; 2351 AA.
XX
AC   AAW10590;
XX
DT   03-DEC-1997  (first entry)
XX
DE   Factor VIII:C (Phe270His).
XX
KW   Factor VIII:C; F8C; Factor V A; Factor V C; domain; F8C deficiency;
KW   haemophilia A; blood clotting disorder; immunogen; antibody.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Peptide          1..19
FT                    /note= "Signal peptide"
FT   Protein          20..2351
FT                    /note= "Mature factor VIII:C"
FT   Misc-difference  289
FT                    /label= Phe270His
XX
PN   WO9703191-A1.
XX
PD   30-JAN-1997.
XX
PF   28-JUN-1996;   96WO-US11013.
XX
PR   11-JUL-1995;   95US-0001030.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Hung DT;
XX
DR   WPI; 1997-119047/11.
XX
PT   Factor VIII:C analogue - modified to comprise Factor V A or C domain
PT   or subdomain, for increased stability or activity
XX
PS   Claim 6; Page -; 45pp; English.
XX
CC   The sequences given in W10590-92 represent active Factor VIII:C (F8C)
CC   polypeptide analogues. These analogues comprises a native F8C
CC   polypeptide modified to comprise the presence of a Factor V A and/or
CC   C domain and/or subdomain. The F8C polypeptide analogues, alone or in
CC   combination, can be used for the prevention or treatment of an active
CC   F8C deficiency, i.e. haemophilia A and other blood clotting disorders.
CC   The analogue can also be used as an immunogen for antibody production.
CC   The analogues can have an increased plasma half-life, or specific
CC   activity. This sequence is not given in the specification and is
CC   based on the sequence derived from Genbank ref. K01740.
XX
SQ   Sequence   2351 AA;

  Query Match          99.8%;  Score 12398;  DB 18;  Length 2351;
  Best Local Similarity   99.9%;  Pred. No. 0;
  Matches 2348;  Conservative    1;  Mismatches    2;  Indels    0;  Gaps    0;

Qy         1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy        61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
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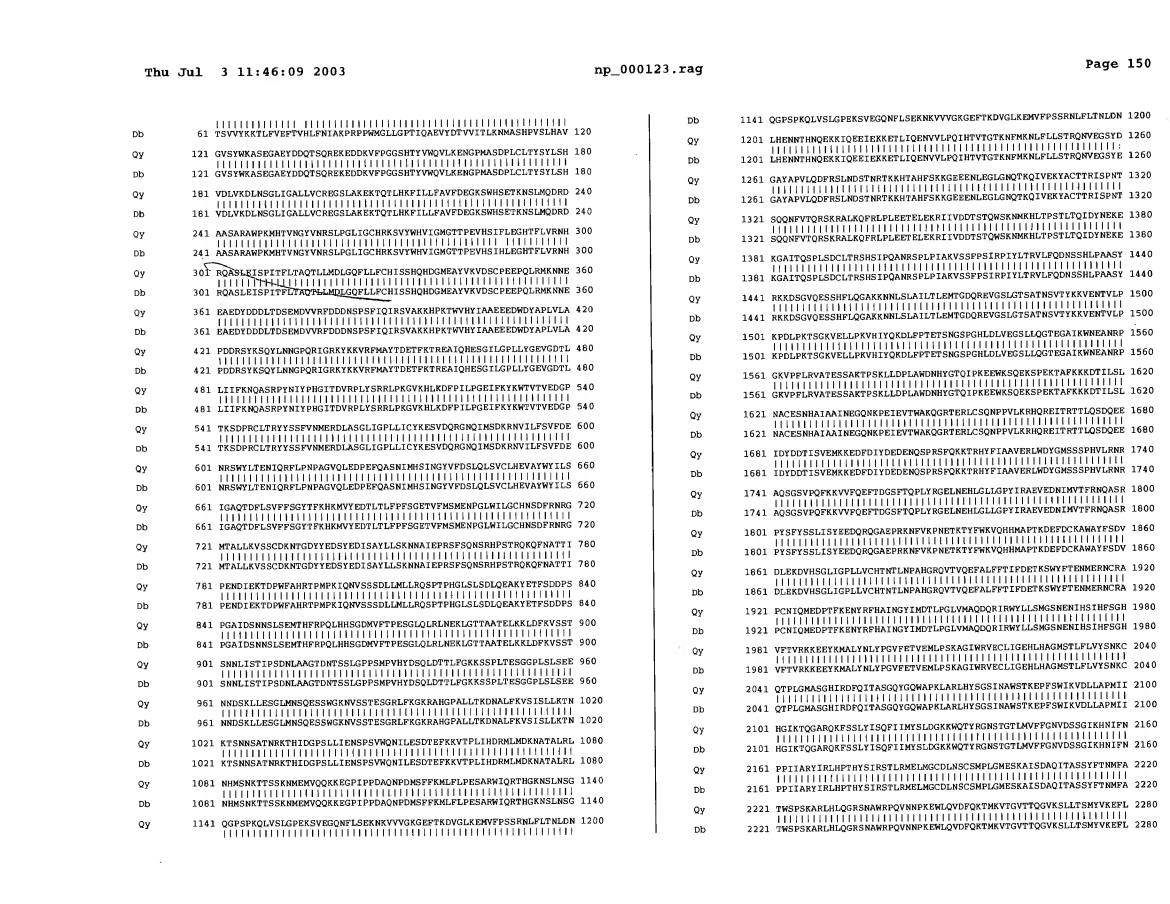

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Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
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Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
             ||||||||||| 
Db       2341 EVLGCEAQDLY 2351


RESULT 92
AAW11405
ID   AAW11405 standard; Protein; 2350 AA.
XX
AC   AAW11405;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue, delta 746, + Q744X.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2350
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1666
FT                   /note= "heavy chain fragment"
FT   Modified-site   763
FT                   /label= Phe, Glu, Pro
FT   Misc-difference 764..765
FT                   /note= "site of 1 residue deletion"
FT   Region          1667..2349
FT                   /note= "light chain fragment"
FT   Domain          759..1666
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 24; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2350 AA;

  Query Match             99.8%;  Score 12397.5;  DB 18;  Length 2350;
  Best Local Similarity   99.9%;  Pred. No. 0.;
  Matches 2349;  Conservative    0;  Mismatches    1;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSXN-RHPSTRQKQFNATTI 779

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        780 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 839
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Qy       841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
Db       840 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFRVSST 899

Qy       901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
Db       900 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 959

Qy       961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
Db       960 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1019

Qy      1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
Db      1020 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1079

Qy      1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
Db      1080 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1139

Qy      1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
Db      1140 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1199

Qy      1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
Db      1200 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1259

Qy      1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
Db      1260 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1319

Qy      1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
Db      1320 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1379

Qy      1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
Db      1380 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1439

Qy      1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
Db      1440 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1499

Qy      1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
Db      1500 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1559

Qy      1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
Db      1560 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1619

Qy      1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
Db      1620 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1679

Qy      1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
Db      1680 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1739

Qy      1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
Db      1740 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1799

Qy      1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
Db      1800 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1859

Qy      1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
Db      1860 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1919

Qy      1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
Db      1920 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1979

Qy      1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
Db      1980 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2039

Qy      2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
Db      2040 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2099

Qy      2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
Db      2100 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2159

Qy      2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
Db      2160 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2219

Qy      2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
Db      2220 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2279

Qy      2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
Db      2280 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2339

Qy      2341 EVLGCEAQDLY 2351
Db      2340 EVLGCEAQDLY 2350
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RESULT 93
AAW11346
ID   AAW11346 standard; Protein; 2350 AA.
XX
AC   AAW11346;
XX
DT   17-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue, delta 251, 252, + Pro insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2350
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1666
FT                   /note= "heavy chain fragment"
FT   Misc-difference 269..270
FT                   /note= "site of 2 residue deletion"
FT   Misc-difference 270
FT                   /note= "inserted residue"
FT   Region          1667..2349
FT                   /note= "light chain fragment"
FT   Domain          759..1666
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11444.
XX
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PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE, Hung DT, Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 11; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence  2350 AA;

  Query Match             99.8%;  Score 12397.5;  DB 18;  Length 2350;
  Best Local Similarity   99.9%;  Pred. No. 0;
  Matches 2349;  Conservative    0;  Mismatches    1;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHR-PVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 299

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        300 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 359

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        360 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 419

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        420 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 479

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        480 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 539

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        540 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 599

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        600 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 659

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        660 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 719

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        720 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 779

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        780 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 839

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        840 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 899

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        900 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 959

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        960 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1019

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1020 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1079

Qy       1081 NHMSNKTTSSKNMEMVQQKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1080 NHMSNKTTSSKNMEMVQQKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1139

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1140 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1199

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1200 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1259

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1260 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1319

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1320 SQQNFVTQRSKRALKQFRLPLEETELEKRIVVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1379

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1380 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1439

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1440 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1499

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1500 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1559

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKDTILSL 1620
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               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1560 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1619

Qy        1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1620 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1679

Qy        1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1680 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1739

Qy        1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1740 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1799

Qy        1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1800 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1859

Qy        1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1860 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1919

Qy        1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1920 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1979

Qy        1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        1980 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2039

Qy        2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2040 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2099

Qy        2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2100 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2159

Qy        2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2160 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2219

Qy        2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2220 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2279

Qy        2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        2280 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2339

Qy        2341 EVLGCEAQDLY 2351
               |||||||||||
Db        2340 EVLGCEAQDLY 2350
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RESULT 94
AAW11470
ID   AAW11470 standard; Protein; 2350 AA.
XX
AC   AAW11470;
XX
DT   21-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue, delta 1720, + L1718X.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2350
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Region          1668..2349
FT                   /note= "light chain fragment"
FT   Domain          759..1667
FT                   /note= "B domain"
FT   Modified-site   1737
FT                   /label= Phe, Glu, Pro
FT   Misc-difference 1738..1739
FT                   /note= "site of 1 residue deletion"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11444.
XX
PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 38; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2350 AA;

  Query Match             99.8%;  Score 12396.5;  DB 18;  Length 2350;
  Best Local Similarity   99.9%;  Pred. No. 0;
  Matches 2349;  Conservative    0;  Mismatches    1;  Indels    1;  Gaps    1;

Qy           1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db           1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy          61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy         121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
```

```
Qy        2341 EVLGCEAQDLY 2351
               ||||||||||| 
Db        2340 EVLGCEAQDLY 2350


RESULT 95
AAW11375
ID   AAW11375 standard; Protein; 2350 AA.
XX
AC   AAW11375;
XX
DT   18-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue, delta 337, 338, + Pro insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2350
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1666
FT                   /note= "heavy chain fragment"
FT   Misc-difference 355..356
FT                   /note= "site of 2 residue deletion"
FT   Misc-difference 356
FT                   /note= "inserted residue"
FT   Region          1667..2349
FT                   /note= "light chain fragment"
FT   Domain          759..1666
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;    96WO-US11444.
XX
PR   11-JUL-1995;    95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 17; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2350 AA;

  Query Match             99.8%;  Score 12396.5;  DB 18;  Length 2350;
  Best Local Similarity   99.9%;  Pred. No. 0;
  Matches 2349;  Conservative    0;  Mismatches    1;  Indels    1;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||| ||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLR-PNNE 359

Qy        361 EADDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        360 EADDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 419

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        420 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 479

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        480 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 539

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        540 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 599

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        600 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 659

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        660 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 719

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        720 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 779

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        780 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 839

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        840 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 899
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Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        900 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 959

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        960 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1019

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1020 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1079

Qy       1081 NHMSNKTTSSKNMEMVQQKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1080 NHMSNKTTSSKNMEMVQQKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1139

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1140 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1199

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1200 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1259

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1260 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1319

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1320 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1379

Qy       1381 KGATTQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1380 KGATTQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1439

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1440 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1499

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1500 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1559

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1560 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1619

Qy       1621 NACESNHAIAAINEGQNKPEIVVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1620 NACESNHAIAAINEGQNKPEIVVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1679

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1680 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1739

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1740 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1799

Qy       1801 PYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1800 PYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1859

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1860 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1919

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1920 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1979

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1980 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2039

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2040 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2099

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2100 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2159

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2160 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2219

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2220 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2279

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2280 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2339

Qy       2341 EVLGCEAQDLY 2351
              ||||||||||| 
Db       2340 EVLGCEAQDLY 2350

RESULT 96
AAR78223
ID   AAR78223 standard; protein; 2351 AA.
XX
AC   AAR78223;
XX
DT   15-NOV-1995  (first entry)
XX
DE   Human Factor-VIII:c.
XX
KW   Factor-VIII:c; blood-clotting; procoagulant; hemophilia;
KW   mutagenesis.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /label= Sig_peptide
FT   Cleavage-site   245..246
FT   Cleavage-site   355..356
FT                   /label= APC_cleavage_site
FT   Cleavage-site   581..582
FT                   /label= APC_cleavage_site
FT   Cleavage-site   717..719
FT                   /label= Factor-Xa_cleavage_site
FT   Cleavage-site   759..760
FT                   /label= 90-kDa_cleavage_site
FT   Cleavage-site   795..796
FT                   /label= 95-kDa_cleavage_site
FT   Cleavage-site   1332..1333
FT                   /label= 115-kDa_cleavage_site
FT   Cleavage-site   1667..1668
FT                   /label= 76-kDa_cleavage_site
FT   Cleavage-site   1740..1741
FT                   /label= Factor-Xa_cleavage_site
XX
PN   US5422260-A.
XX
PD   06-JUN-1995.
XX
PF   29-MAY-1986;    86US-0868410.
XX
PR   02-DEC-1988;    88US-0279485.
PR   29-MAY-1986;    86US-0868410.
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PR   18-NOV-1986;   86US-0932767.
PR   09-DEC-1986;   86US-0939658.
PR   15-MAY-1992;   92US-0883936.
XX
PA   (GEMY ) GENETICS INST INC.
XX
PI   Kaufman RJ,  Pittman DD,  Toole JJ;
XX
DR   WPI; 1995-214657/28.
XX
PT   New human factor VIII:c mutein(s) - useful for treating or preventing
PT   bleeding disorders
XX
PS   Disclosure; Fig.1; 16pp; English.
XX
CC   The sequence of natural human Factor-VIII:c is given in AAR78223.
CC   Mutagenesis of cDNA encoding the protein, resulting in deletion
CC   or substn. of key amino acid residues, allows prodn. of Factor-
CC   VIII:c muteins with reduced lability for protease-catalyzed
CC   cleavage but with retained procoagulant activity.
XX
SQ   Sequence   2351 AA;

  Query Match             99.8%;  Score 12396;  DB 16;  Length 2351;
  Best Local Similarity   99.9%;  Pred. No. 0;
  Matches 2348;  Conservative    1;  Mismatches    2;  Indels    0;  Gaps    0;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTVHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITPRTLQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITPLTLQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYE 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
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Qy       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 TWSPSKARLHLQGRSNAWRPQVNNHKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
                ||||||||||
Db       2341 EVLGCEAQDLY 2351


RESULT 97
AAW11460
ID   AAW11460 standard; Protein; 2349 AA.
XX
AC   AAW11460;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue residue 1716, 1717 deletion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2349
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Region          1668..2348
FT                   /note= "light chain fragment"
FT   Domain          760..1667
FT                   /note= "B domain"
FT   Misc-difference 1734..1735
FT                   /note= "site of 2 residue deletion"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11444.
XX
PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 36; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2349 AA;

  Query Match             99.8%;  Score 12395;  DB 18;  Length 2349;
  Best Local Similarity   99.9%;  Pred. No. 0;
  Matches 2349;  Conservative    0;  Mismatches    0;  Indels    2;  Gaps    1;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
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Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Db       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
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Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKDTILSL 1620

Db       1561 GKVPFLAVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSPQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSPQKKTRHYFIAAVERLWDYGMSSSP--LRNR 1738

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Db       1739 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1798

Qy       1801 PYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Db       1799 PYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1858

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920

Db       1859 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1918

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Db       1919 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1978

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Db       1979 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2038

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Db       2039 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2098

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Db       2099 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2158

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Db       2159 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2218

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Db       2219 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2278

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Db       2279 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2338

Qy       2341 EVLGCEAQDLY 2351

Db       2339 EVLGCEAQDLY 2349

RESULT 98
AAR55352
ID   AAR55352 standard; Protein; 2351 AA.
XX
AC   AAR55352;
XX
DT   10-NOV-1994  (first entry)
XX
DE   Sequence of human factor VIII.
XX
```

```
KW   Factor VIII; haemostasis; haemophilia A; clotting cascade;
KW   fibrinogen; fibrin; thrombin; proteolytic enzyme; co-factor.
XX
OS   Homo sapiens.
XX
PN   WO9411503-A.
XX
PD   26-MAY-1994.
XX
PF   01-OCT-1993;    93WO-US09438.
XX
PR   13-NOV-1992;    92US-0976086.
PR   14-SEP-1993;    93US-0121202.
XX
PA   (GEMY ) GENETICS INST INC.
XX
PI   Kaufman RJ,  Pittman D,  Rehemtulla A,  Wozney JM;
XX
DR   WPI; 1994-183504/22.
DR   N-PSDB; AAQ66615.
XX
PT   Nucleic acid encoding porcine factor VIII - used to obtain
PT   porcine and human-porcine chimeric factor VIII for treating
PT   haemophilia
XX
PS   Disclosure; Page 27-36; 61pp; English.
XX
CC   Prepn. of human factor VIII cDNA has been set forth in detail, e.g.,
CC   US Patent No. 4,757,006 issued July 12, 1988 and in Toole et al.,
CC   Nature 312:312(1984). A recombinant clone comprg. the nucleotide
CC   sequence in AAQ66615, designated as pSP64-VIII, is on deposit at the
CC   ATTC under Accession No. ATCC 39812. Chimeric forms of factor VIII
CC   include those where various domains of the human factor VIII have
CC   been replaced, in whole or in part, by analogous porcine factor VIII
CC   domains, and include, chimeric forms where the A1 and/or A2 domains,
CC   in whole or in part, of the human factor VIII sequence have been
CC   replaced, in whole or in part, by the A1 and/or the A2 domains of
CC   porcine factor VIII. Specifically provided are chimeric factor VIII
CC   sequences comprising the A1, A2, A3, B, C1 and C2 human domains  as
CC   set forth in AAQ66615, where the A1 and/or A2 domains, as well as
CC   other segments, such as the regions corresp. to the AA numbers
CC   336-372, 336-740, 372-740, 700-740 and combinations of these
CC   regions have been replaced in whole or in part with porcine factor
CC   VIII sequences as set forth in AAQ66616 and AAR53353.
XX
SQ   Sequence   2351 AA;

  Query Match             99.8%;  Score 12395;  DB 15;  Length 2351;
  Best Local Similarity   99.9%;  Pred. No. 0;
  Matches 2348;  Conservative    1;  Mismatches    2;  Indels    0;  Gaps    0;

Qy          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy         61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TSVVYKKTLFVEFTVHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360

Qy        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420

Qy        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480

Qy        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKTLKDFPILPGEIFKYKWTVTVEDGP 540

Qy        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600

Qy        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660

Qy        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720

Qy        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Qy        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Qy       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYE 1260

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Qy       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
```

```
Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Qy       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQREITRTTLQSDQEE 1680

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Qy       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAFFSDV 1860
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAFFSDV 1860

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCRA 1920
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFPTIFDETKSWYFTENMERNCRA 1920

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Qy       2341 EVLGCEAQDLY 2351
                ||||||||||
Db       2341 EVLGCEAQDLY 2351


RESULT 99
AAW11457
ID   AAW11457 standard; Protein; 2350 AA.
XX
AC   AAW11457;
XX
DT   20-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue, delta 1720, 1721, + Pro insertion.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2350
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1667
FT                   /note= "heavy chain fragment"
FT   Region          1668..2349
FT                   /note= "light chain fragment"
FT   Domain          759..1667
FT                   /note= "B domain"
FT   Misc-difference 1738..1739
FT                   /note= "site of 2 residue deletion"
FT   Misc-difference 1739
FT                   /note= "inserted residue"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11444.
XX
PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE, Hung DT, Innis M;
XX
DR   WPI: 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 35; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAY51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2350 AA;

  Query Match           99.8%;  Score 12394.5;  DB 18;  Length 2350;
  Best Local Similarity   99.9%;  Pred. No. 0;
  Matches 2349;  Conservative    0;  Mismatches    1;  Indels    1;  Gaps    1;
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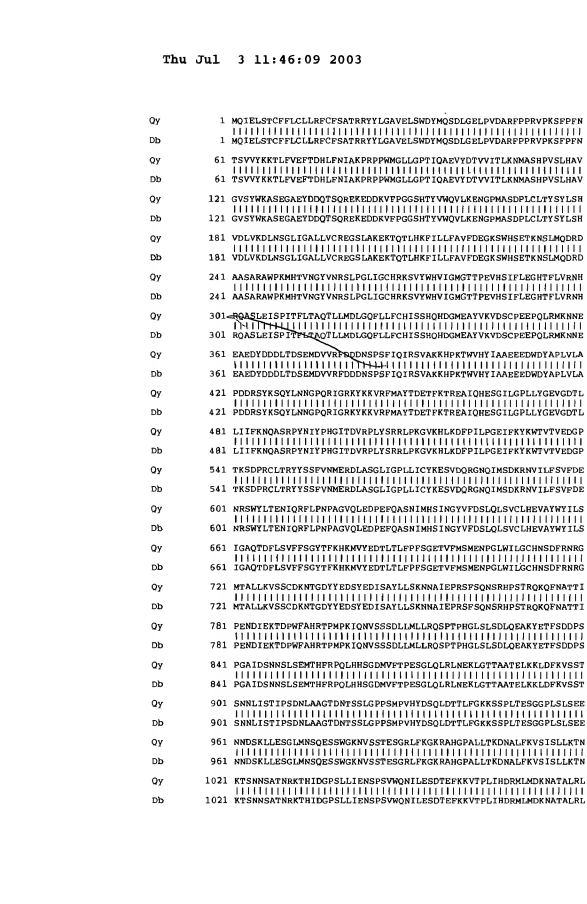
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Db 1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
Qy 61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
Db 61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
Qy 121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
Db 121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
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Db 181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
Qy 241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
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Qy 301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
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Db 361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
Qy 421 PDDRSYKSQTLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
Db 421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
Qy 481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
Db 481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
Qy 541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
Db 541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
Qy 601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
Db 601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
Qy 661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
Db 661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
Qy 721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
Db 721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
Qy 781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
Db 781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840
Qy 841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
Db 841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900
Qy 901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
Db 901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960
Qy 961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLFKDNALFKVSISLLKTN 1020
Db 961 NNDSKLLESGLMNSQESSWGKNVSSTESGRLFKGKRAHGPALLFKDNALFKVSISLLKTN 1020
Qy 1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
Db 1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080
Qy 1081 NHMSNKTTSSKNMEMVQQKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
Db 1081 NHMSNKTTSSKNMEMVQQKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140
Qy 1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
Db 1141 QGPSPKQLVSLGPEKSVEGQNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200
Qy 1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
Db 1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260
Qy 1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKTACTRISPNT 1320
Db 1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320
Qy 1321 SQQNVFTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYENKE 1380
Db 1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYENKE 1380
Qy 1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
Db 1381 KGAITQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440
Qy 1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
Db 1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500
Qy 1501 KPDLPKTSGKVELLPKVHIYQKDLFPTEVSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
Db 1501 KPDLPKTSGKVELLPKVHIYQKDLFPTEVSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560
Qy 1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620
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Qy 1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740
Db 1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLR-P 1739
Qy 1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800
Db 1740 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1799
Qy 1801 PYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860
Db 1800 PYSFYSSLISYEEDQRQAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1859
Qy 1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920
Db 1860 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1919
Qy 1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980
Db 1920 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1979
Qy 1981 VFTVKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040
Db 1980 VFTVKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2039
Qy 2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100
Db 2040 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2099
Qy 2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160
Db 2100 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2159
Qy 2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

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                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         2160 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2219

Qy         2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         2220 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2279

Qy         2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         2280 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2339

Qy         2341 EVLGCEAQDLY 2351
                |||||||||||
Db         2340 EVLGCEAQDLY 2350


RESULT 100
AAW11380
ID   AAW11380 standard; Protein; 2350 AA.
XX
AC   AAW11380;
XX
DT   18-NOV-1997  (first entry)
XX
DE   Active Factor VIII:C analogue, delta 335, + P333X.
XX
KW   Factor VIII:C; analogue; glycoprotein; blood coagulation cascade;
KW   fibrinogen; fibrin clot; haemostasis; haemophilia A; bleeding diathesis;
KW   plasma protease; thrombin; immunogen; antibody; haemophiliac; therapy;
KW   proteolytic cleavage.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..19
FT                   /note= "signal peptide"
FT   Protein         20..2350
FT                   /note= "mature Factor VIII:C"
FT   Region          20..1666
FT                   /note= "heavy chain fragment"
FT   Modified-site   352
FT                   /label= Phe, Glu
FT   Misc-difference 353..354
FT                   /note= "site of 1 residue deletion"
FT   Region          1667..2349
FT                   /note= "light chain fragment"
FT   Domain          759..1666
FT                   /note= "B domain"
XX
PN   WO9703195-A1.
XX
PD   30-JAN-1997.
XX
PF   09-JUL-1996;   96WO-US11444.
XX
PR   11-JUL-1995;   95US-0001025.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cohen FE,  Hung DT,  Innis M;
XX
DR   WPI; 1997-119050/11.
XX
PT   Factor VIII:C analog modified adjacent to a non-activating Arg
PT   residue - used in the treatment of haemophiliacs, by improvement of
PT   haemostasis
XX
PS   Claim 18; Page -; 90pp; English.
XX
CC   AAW11330-W11472 represent active Factor VIII:C analogues of the
CC   invention. These sequences were created by mutating the wild type Factor
CC   VIII:C coding sequence (see AAT51357) using mutagenic primers. The
CC   analogues comprise a native Factor VIII:C polypeptide modified at a site
CC   adjacent to a non-activating Arg residue so that a Arg-Pro or Pro-Arg
CC   dipeptide is created. Factor VIII:C is a large glycoprotein that
CC   participates in the blood coagulation cascade that ultimately converts
CC   soluble fibrinogen to insoluble fibrin clot, effecting haemostasis. A
CC   deficiency in Factor VIII:C is responsible for haemophilia A, which is an
CC   X-chromosome-linked inherited bleeding diathesis. Factor VIII:C is
CC   activated by plasma proteases, such as thrombin. During activation the
CC   mature polypeptide is cleaved to generate heavy and light chain fragments
CC   that are further cleaved. Complexes of two or more of the analogues,
CC   nucleic acids and vectors encoding them may be used alone or in
CC   conjunction with each other, for the prevention or treatment of active
CC   Factor VIII:C deficiency in a mammal. The analogues may be used as
CC   immunogens to raise antibodies, and in the treatment of haemophiliacs, by
CC   improvement of haemostasis. The analogues are resistant to proteolytic
CC   cleavage and display increased plasma half-life. They may be administered
CC   at lower dosages and by different modes of administration.
XX
SQ   Sequence   2350 AA;

  Query Match             99.8%;  Score 12394.5;  DB 18;  Length 2350;
  Best Local Similarity   99.9%;  Pred. No. 0;
  Matches 2349;  Conservative    0;  Mismatches    1;  Indels    1;  Gaps    1;

Qy            1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db            1 MQIELSTCFFLCLLRFCFSATRRYYLGAVELSWDYMQSDLGELPVDARFPPRVPKSFPFN 60

Qy           61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db           61 TSVVYKKTLFVEFTDHLFNIAKPRPPWMGLLGPTIQAEVYDTVVITLKNMASHPVSLHAV 120

Qy          121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          121 GVSYWKASEGAEYDDQTSQREKEDDKVFPGGSHTYVWQVLKENGPMASDPLCLTYSYLSH 180

Qy          181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          181 VDLVKDLNSGLIGALLVCREGSLAKEKTQTLHKFILLFAVFDEGKSWHSETKNSLMQDRD 240

Qy          241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          241 AASARAWPKMHTVNGYVNRSLPGLIGCHRKSVYWHVIGMGTTPEVHSIFLEGHTFLVRNH 300

Qy          301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEPQLRMKNNE 360
                |||||||||||||||||||||||||||||||||||||||||||||||||| | ||||||
Db          301 RQASLEISPITFLTAQTLLMDLGQFLLFCHISSHQHDGMEAYVKVDSCPEEXQ-RMKNNE 359

Qy          361 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 420
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          360 EAEDYDDDLTDSEMDVVRFDDDNSPSFIQIRSVAKKHPKTWVHYIAAEEEDWDYAPLVLA 419

Qy          421 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 480
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          420 PDDRSYKSQYLNNGPQRIGRKYKKVRFMAYTDETFKTREAIQHESGILGPLLYGEVGDTL 479

Qy          481 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 540
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          480 LIIFKNQASRPYNIYPHGITDVRPLYSRRLPKGVKHLKDFPILPGEIFKYKWTVTVEDGP 539

Qy          541 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 600
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          540 TKSDPRCLTRYYSSFVNMERDLASGLIGPLLICYKESVDQRGNQIMSDKRNVILFSVFDE 599

Qy          601 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 660
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          600 NRSWYLTENIQRFLPNPAGVQLEDPEFQASNIMHSINGYVFDSLQLSVCLHEVAYWYILS 659

Qy          661 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 720
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          660 IGAQTDFLSVFFSGYTFKHKMVYEDTLTLFPFSGETVFMSMENPGLWILGCHNSDFRNRG 719

Qy          721 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 780
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Db        720 MTALLKVSSCDKNTGDYYEDSYEDISAYLLSKNNAIEPRSFSQNSRHPSTRQKQFNATTI 779

Qy        781 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 840

Db        780 PENDIEKTDPWFAHRTPMPKIQNVSSSDLLMLLRQSPTPHGLSLSDLQEAKYETFSDDPS 839

Qy        841 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 900

Db        840 PGAIDSNNSLSEMTHFRPQLHHSGDMVFTPESGLQLRLNEKLGTTAATELKKLDFKVSST 899

Qy        901 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 960

Db        900 SNNLISTIPSDNLAAGTDNTSSLGPPSMPVHYDSQLDTTLFGKKSSPLTESGGPLSLSEE 959

Qy        961 NNDSKLLESGLWNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1020

Db        960 NNDSKLLESGLWNSQESSWGKNVSSTESGRLFKGKRAHGPALLTKDNALFKVSISLLKTN 1019

Qy       1021 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1080

Db       1020 KTSNNSATNRKTHIDGPSLLIENSPSVWQNILESDTEFKKVTPLIHDRMLMDKNATALRL 1079

Qy       1081 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1140

Db       1080 NHMSNKTTSSKNMEMVQQKKEGPIPPDAQNPDMSFFKMLFLPESARWIQRTHGKNSLNSG 1139

Qy       1141 QGPSPKQLVSLGPEKSVEQGNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1200

Db       1140 QGPSPKQLVSLGPEKSVEQGNFLSEKNKVVVGKGEFTKDVGLKEMVFPSSRNLFLTNLDN 1199

Qy       1201 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1260

Db       1200 LHENNTHNQEKKIQEEIEKKETLIQENVVLPQIHTVTGTKNFMKNLFLLSTRQNVEGSYD 1259

Qy       1261 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1320

Db       1260 GAYAPVLQDFRSLNDSTNRTKKHTAHFSKKGEEENLEGLGNQTKQIVEKYACTTRISPNT 1319

Qy       1321 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1380

Db       1320 SQQNFVTQRSKRALKQFRLPLEETELEKRIIVDDTSTQWSKNMKHLTPSTLTQIDYNEKE 1379

Qy       1381 KGATIQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1440

Db       1380 KGATIQSPLSDCLTRSHSIPQANRSPLPIAKVSSFPSIRPIYLTRVLFQDNSSHLPAASY 1439

Qy       1441 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1500

Db       1440 RKKDSGVQESSHFLQGAKKNNLSLAILTLEMTGDQREVGSLGTSATNSVTYKKVENTVLP 1499

Qy       1501 KPDLPKTSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1560

Db       1500 KPDLPKPSGKVELLPKVHIYQKDLFPTETSNGSPGHLDLVEGSLLQGTEGAIKWNEANRP 1559

Qy       1561 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1620

Db       1560 GKVPFLRVATESSAKTPSKLLDPLAWDNHYGTQIPKEEWKSQEKSPEKTAFKKKDTILSL 1619

Qy       1621 NACESNHAIAAINEGQNKPEISVTWAKQGRTERLCSQNPPVLKRHQRETRTTLQSDQEE 1680

Db       1620 NACESNHAIAAINEGQNKPEIEVTWAKQGRTERLCSQNPPVLKRHQRETRTTLQSDQEE 1679

Qy       1681 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1740

Db       1680 IDYDDTISVEMKKEDFDIYDEDENQSPRSFQKKTRHYFIAAVERLWDYGMSSSPHVLRNR 1739

Qy       1741 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1800

Db       1740 AQSGSVPQFKKVVFQEFTDGSFTQPLYRGELNEHLGLLGPYIRAEVEDNIMVTFRNQASR 1799

Qy       1801 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1860

Db       1800 PYSFYSSLISYEEDQRQGAEPRKNFVKPNETKTYFWKVQHHMAPTKDEFDCKAWAYFSDV 1859

Qy       1861 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1920

Db       1860 DLEKDVHSGLIGPLLVCHTNTLNPAHGRQVTVQEFALFFTIFDETKSWYFTENMERNCRA 1919

Qy       1921 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1980

Db       1920 PCNIQMEDPTFKENYRFHAINGYIMDTLPGLVMAQDQRIRWYLLSMGSNENIHSIHFSGH 1979

Qy       1981 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2040

Db       1980 VFTVRKKEEYKMALYNLYPGVFETVEMLPSKAGIWRVECLIGEHLHAGMSTLFLVYSNKC 2039

Qy       2041 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2100

Db       2040 QTPLGMASGHIRDFQITASGQYGQWAPKLARLHYSGSINAWSTKEPFSWIKVDLLAPMII 2099

Qy       2101 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2160

Db       2100 HGIKTQGARQKFSSLYISQFIIMYSLDGKKWQTYRGNSTGTLMVFFGNVDSSGIKHNIFN 2159

Qy       2161 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2220

Db       2160 PPIIARYIRLHPTHYSIRSTLRMELMGCDLNSCSMPLGMESKAISDAQITASSYFTNMFA 2219

Qy       2221 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2280

Db       2220 TWSPSKARLHLQGRSNAWRPQVNNPKEWLQVDFQKTMKVTGVTTQGVKSLLTSMYVKEFL 2279

Qy       2281 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2340

Db       2280 ISSSQDGHQWTLFFQNGKVKVFQGNQDSFTPVVNSLDPPLLTRYLRIHPQSWVHQIALRM 2339

Qy       2341 EVLGCEAQDLY 2351

Db       2340 EVLGCEAQDLY 2350
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Search completed: July 2, 2003, 15:28:11
Job time : 166 secs